

*W.B.*

NOT TO BE TAKEN AWAY

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*Supplement to the "F.M.S. Government Gazette," October 9, 1914.*

## FEDERATED MALAY STATES.

## MEDICAL REPORT FOR THE YEAR 1913.

## VITAL STATISTICS.

The estimated population of the Federated Malay States for the year 1913 is returned at 1,117,625.

The number of deaths 38,000, giving a death-rate of 34.0 per mille as against 40,901 and a death-rate of 37.8 per mille in 1912.

## BIRTHS.

Total births registered were 26,349. The birth-rate is therefore 23.05 per mille.

Compared with 1912 the following nationalities show an increase:

						Increase.	Decrease.
Europeans	...	...	...	...	...	...	.65
Eurasians	...	...	...	...	...	1.46	
Chinese	...	...	...	...	...	1.72	
Malays	...	...	...	...	...	...	3.28
Indians	...	...	...	...	...	4.17	

## MEDICAL INSTITUTIONS.

		Hospitals.	Gaol hospitals.	Lunatic asylums.	Leper asylums.
Perak	...	16	3	1	2
Selangor	...	12	1	1	1
Negri Sembilan	...	7	1		
Pahang	...	5	4		
Total	...	40	9	2	3

The number of in-patients treated was:

		Number treated.	Deaths.	Per cent.
Perak	...	45,349	3,670	8.09
Selangor	...	32,173	3,154	9.8
Negri Sembilan	...	17,064	1,451	8.50
Pahang	...	6,074	378	6.22
Total	...	100,660	8,653	

an increase of 3,498 on the previous year.

The following list gives details of nationalities:

	Perak.		Selangor.		Negri Sembilan.		Pahang.		Total.	
	1912.	1913.	1912.	1913.	1912.	1913.	1912.	1913.	1912.	1913.
Europeans ...	170	203	305	357	105	133	11	19	591	712
Eurasians ...	54	75	126	148	29	50	10	8	219	281
Chinese ...	22,121	24,217	16,935	15,559	9,787	9,903	2,462	2,939	51,305	52,618
Malays ...	2,137	2,142	1,136	1,228	954	919	894	978	5,121	5,267
Indians ...	17,447	18,598	12,157	13,114	6,425	5,871	1,992	2,072	38,021	39,655
Others ...	138	114	1,512	1,767	99	188	156	58	1,905	2,127
Total ...	42,067	45,349	32,171	32,173	17,399	17,064	5,525	6,074	97,162	100,660

Out-patient attendances = 251,590

		Hospitals and dispensaries.	Travelling dispensaries.
Perak ...	...	74,817	49,769
Selangor ...	...	66,907	
Negri Sembilan ...	...	31,278	668
Pahang ...	...	26,210	1,941
Total ...	...	199,212	52,378

an increase of 5,819 over 1912.

Two thousand five hundred and sixty Malays attended the Kuala Pilah Hospital as out-patients.

## LUNATIC ASYLUMS.

Six hundred and ninety-six lunatics were under treatment during the year, and there were 57 deaths.

The Superintendent, Central Lunatic Asylum—Dr. Samuels—*inter alia* reports as follows:

Again melancholia was the most frequent form of disease, while general paralysis of the insane is still well represented.

Hitherto all the cases of general paralysis of the insane admitted have been Chinese, but this year we admitted one Malay.

Some of the cases, particularly in the later stages, were very typical.

There was one suicide in January, but since then I am thankful to say we have been free, though the attempts were as numerous as ever. I think I am safe in saying that the attendants at last appreciate the seriousness of the occurrence in the wards.

The recovery rate is only 20.67 per cent., but here account must be taken of the number of transfers admitted, the great majority of whom were hopeless, being either chronic or even demented. Many of them had been insane for years.

The system of collecting cases in various centres and then sending them in great batches is extremely bad. Not only is there a risk of their becoming demented or chronic the longer they are untreated but a proper examination of each case is out of the question, also the cases tend to lose their identity immediately, which is a thing to be avoided.

The disadvantage of collecting patients and sending in batches can be seen from the recovery rate for transfers and for direct admissions.

Transfers ...	...	...	...	...	...	4.67 per cent. (males)
Direct admissions ...	...	...	...	...	...	35.95     ,     ,

While on the female side where there were no transfers the recovery rate was 43.18 per cent.

When the acute wards are built the recovery rate should improve as we shall not then have the acute mental cases mixed up with the old chronic and feeble cases, and more time can be given to the treatment of the acute cases, who will have special attendants to look after them.

We have again a large number of criminals sent us, but I have now turned No. VI into a criminal ward, so that this class of patient does not mix with the others, but of course tends to increase the overcrowding; and, on recovery, which sometimes takes place, the gaol authorities are loth to take them back, and have to be frequently reminded of the fact that a sane criminal is detained in the asylum.

The death-rate was 8.18 per cent. Dysentery accounted for 4.31 per cent.

We have been fighting dysentery all the year, and have also had to contend with cases being transferred suffering from the disease. Each batch we received from Kuala Lumpur had cases of dysentery in it.

Again on the female side with no transfers there were no deaths from dysentery, and only two very mild cases.

A glance at the aetiological table shows malaria appearing, either as a principal or contributory factor, on 31 occasions. Alcohol comes next with 19. Drugs (opium four times) appears five times, and I only once saw typical deprivation symptoms.

The forms which are sent out to patients' friends have proved quite satisfactory. Many, however, are returned by the post office "addressee unknown," but of those that reach their destination the great majority are filled up and returned.

At the end of October the farm built by the patients was completed. This accommodates 15 patients with an attendant. They live altogether here doing their own cooking, etc. They are extremely happy, as a visit to them shows, and work extremely well. They look after the pigs and ducks as well as gardening.

The pig-sty was built by the patients, it has a cement floor under planks and a cement drain.

The duck pond has been arranged with sluice gates so that it can be filled and emptied at will, and is emptied at night when the ducks are shut up. It is fed from a stream which flows besides the pond wall, and is afterwards drained into the main drain at the back of the asylum.

Fifteen small pigs were purchased from savings on "Diets and Extras," which was re-voted as "Purchase of Pigs for a Piggery, Central Lunatic Asylum," and I hope this year to be able to supply pork to the patients.

The ducks—we have made a start with 20—were bought out of savings on "Diets and Extras."



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The cattle (six cows and a bull) purchased in India arrived on 21st October, 1913. The first calved on 26th October, and the next a month later. Altogether four have calved now. A seventh cow was bought in Ipoh with calf. She has not been so successful as the Indian cows, and gives little milk.

All the calves with one exception are bulls.

I attach a list of produce supplied by the farm worth \$616.09. Only eggs actually supplied to the patients are included. Those used for hatching are not included. The bananas on the female side did particularly well. Some suckers planted in April actually bore in August. Few of the bunches were less than eight-hand ones.

As time goes on I hope to increase this very largely, and to supply all the vegetables consumed by the patients, and a large proportion of the milk.

The patients did a very large amount of work during the year; as well as clearing and draining, which is proceeding steadily ; they built the cattle-shed, farm-house with kitchen, etc., pig-sty, duck-house and the pond, etc.

The Clerk of Works, Public Works Department, Ipoh, kindly valued these buildings for me and puts it down at \$1,292.00—I enclose his estimate. The only articles purchased were nails, split rattan, cement and some of the planks.

The female patients made all the patients' clothing, as well as the female attendants' uniforms, pillows, etc., with a large amount of mending. We now purchase blue khaki drill, and have the male attendants' uniform made in the village, while the female attendants' uniform is now made out of the same material, and is made in the work-room. By this means a considerable saving has been effected.

I attach a list of work done in the work-room.

The proportion of working patients is:

Male ... ... ... ... ... ... ... ... ... 67 and  
 Female ... ... ... ... ... ... ... ... ... .60

No work except what is absolutely necessary is done on Sunday, the patients go instead for a walk round the grounds and some of the better ones go to the town.

The patients are supplied with cards, dominoes, etc., which they use during the non-working hours. Football is indulged in every day during the season by patients and attendants, while I also started cricket during the year.

The maintenance charge works out at \$86.30 per annum. If, however, we subtract \$1,073 spent in furniture for the new wards, etc., which usually would be paid from a special equipment vote, the cost is only \$83.76.

The annual athletic sports were held on 11th July, and were again a great success.

The attendants have been on the whole satisfactory and I hope at last we are building up a reliable staff.

The head attendants on both sides have worked extremely well, and under the Dressers and Matron, respectively, have maintained excellent discipline, and have guarded the interests of the patients.

Lectures have been held weekly since June last, and the first examination will be held shortly. I hope Government will see its way to grant a small allowance in future to those who pass.

Of the attendants the Chinese are the most intelligent, but they are hard to get and do not, as a rule, take kindly to discipline. Bengalis can be got without the least trouble; of them, by far the most satisfactory in every way are the Brahmims. Tamils are fairly easily got and are fairly satisfactory.

The Malaria Institute has a good deal to do. On the one side there

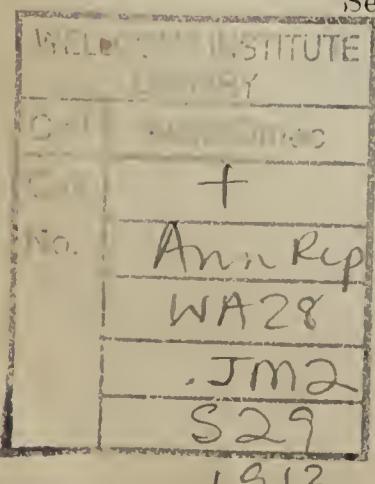
The Malays are, I am sorry to say, not a success as attendants. On the male side they have been a complete failure, while on the female side they have been little better. When one gets a promising one he leaves for some reason or other as soon as he is becoming useful, and as often as not leaves without notice.

I am glad to say that a beginning has been made with an After-care Association. At present it merely consists of a promise from a number of the leading Towkays in Ipoli to help to procure work for discharged patients, who have nowhere to go on discharge.

## LEPER ASYLUMS.

There were 762 cases under treatment, three repatriated, 37 absconded, and 143 died.

		Treated.	Repatriated.	Absconded.	Died
Perak	...	100	3	3	13
Pulan Jerejak	...	252	...	...	84
Pulan Pankor	...	64	...	...	10
Selangor	...	346	...	34	36
E	Total	762	3	37	143



## ZYMOTIC DISEASES.

Outbreak of small-pox occurred in Perak : there were 134 cases and 38 deaths ; nearly all of them were notified at Chemor, Temoh and Kota Bahru. Energetic measures were undertaken to check the spread of the disease.

SMALL-POX.										
Selangor	...	...	...	...	...	...	...	...	...	43
Negri Sembilan	...	...	...	...	...	...	...	...	...	7
Pahang	...	...	...	...	...	...	...	...	...	36
CHICKEN-POX.										
Perak	...	...	...	...	...	...	...	...	...	14
Selangor	...	...	...	...	...	...	...	...	...	17
Negri Sembilan	...	...	...	...	...	...	...	...	...	9
Pahang	...	...	...	...	...	...	...	...	...	3
MEASLES.										
Perak	...	...	...	...	...	...	...	...	...	28
Selangor	...	...	...	...	...	...	...	...	...	25
Negri Sembilan	...	...	...	...	...	...	...	...	...	112
Pahang	...	...	...	...	...	...	...	...	...	277
MUMPS.										
Perak	...	...	...	...	...	...	...	...	...	15
Selangor	...	...	...	...	...	...	...	...	...	9
Negri Sembilan	...	...	...	...	...	...	...	...	...	14
Pahang	...	...	...	...	...	...	...	...	...	—
DYSENTERY.										
Perak	...	...	...	...	...	...	...	...	...	2,991
Selangor	...	...	...	...	...	...	...	...	...	1,455
Negri Sembilan	...	...	...	...	...	...	...	...	...	854
Pahang	...	...	...	...	...	...	...	...	...	259
								Total	...	5,559

a decrease of 1,666 over previous year.

The incidence of both dysentery and enteric requires careful watching—there is reason to believe that the improvement of water supplies is having good results. During the year a notice was widely issued warning people against the risk of eating uncooked vegetables which are grown by Chinese gardeners whose methods of cultivation are not cleanly.

		Enteric cases.	Died.
Perak	...	...	4
Selangor	...	...	12
Negri Sembilan	...	...	—
Pahang	...	...	1
	Total	60	17

The figures for 1912 were 66 cases with 20 deaths.

## PHthisis.

There were 1,771 cases of phthisis treated with 884 deaths in 1913 as against 2,542 cases in 1912.

The prevalence of this disease is still a matter of concern ; the number of cases treated in hospital do not give a complete record of it—as far as can be ascertained it appears that cases occur amongst all races, whether living in towns or country—a recent investigation in a few Malay kampongs disclosed the fact that a certain number were tuberculous. The reasons for the distribution of phthisis in this country are not easy to discover ; a recent theory that the descendants of people infected with syphilis possess tissues particularly suitable to the growth and development of the bacillus of tubercle would, if proved correct, go a long way towards explaining it. Most officers who have had long experience in this country emphatically declare that the disease does not as a rule respond well to treatment.

## CHOLERA.

Twenty-six cases occurred in Perak and Selangor with 17 deaths.

## YAWS.

Sixty-four cases were treated in the various hospitals throughout the Federated Malay States.

## BERI-BERI.

Six thousand four hundred and nine cases with 716 deaths as compared with 5,676 and 657 deaths during the previous year.

The price of tin has dropped and a large number of Chinese labourers will be obliged to live more economically whilst the depression continues, therefore it is not improbable that the proportion of cases will increase somewhat in the near future.

## MALARIA.

Sixteen thousand four hundred and fourteen people died from this disease during the year as against 17,870 in 1912.

The report of the Malaria Advisory Board is attached ; it will be seen that considerable benefit has been obtained as a result of what has been done ; had a larger staff been available important work would not have been delayed and still more relief secured. Now it is known that anti-malarial work can be economically carried out and good results certainly follow it, there is no reason why the disease should continue to be such a menace to the population, the record of deaths is bad enough, but it must also be remembered that each death represents many attacks of fever, much suffering, considerable individual and public expense, besides interference with business. The Malaria Advisory Board has shown how work can be done by systematic and effective methods properly directed and controlled. With a record such as is disclosed there appears to be no excuse for delaying immediate operation on an extensive scale, the expense is shown to be moderate and the gain would be enormous. It is only right that Government should proceed cautiously when spending money on what might be considered experimental efforts, but now that certain anti-malarial measures have been tested and shown to be efficacious, no efforts should be spared and no expense considered too great to remove such a curse and drawback to these States. But I cannot impress upon Government too strongly the absolute necessity for the exercise of careful control over anti-malarial operations and the need of providing adequate means to carry them out accurately and thoroughly by trained skilled individuals. Good work has been done on several estates and much is in progress, general interest in the subject of prevention of malaria has spread, and there is every reason to expect an increase in the number of undertakings in the near future ; the anti-malarial work done by those responsible for estates is most creditable as it often meant many difficulties to face and an extra burden of work and responsibility, in some cases preliminary failures have not daunted a man who is determined to provide a healthy area for his labourers to live in ; fortunately, well deserved success eventually rewards plucky efforts. When certain drainage works on estates have stood the test of time, it will be possible to publish figures and results ; those already received, in the majority of instances, are very encouraging.

## ESTATES.

One of the most gratifying features of the year 1913 is the reduction of the death-rate amongst estate labourers :

In 1911 the rate was	...	...	...	...	...	...	...	62.95
" 1912	"	...	...	...	...	...	...	41.02
" 1913	"	...	...	...	...	...	...	29.6

General vital statistics in this country are not reliable, population varies according to demands of the two principal industries—viz., rubber growing and tin mining, and therefore it is improbable that anything like a correct estimate is made yearly, but in the case of estate labourers accurate returns are available, consequently the estate mortality rate can be accepted with confidence.

During 1911 and early in 1912, endeavours were made to encourage estate managers to pay special attention to various drawbacks to the health of Indian labourers ; these endeavours were received cordially and acted upon largely ; the results have been excellent, the condition of sanitation, housing, water supply, and the sick are very much improved, more care is taken over recruiting and the system of detaining immigrant labourers for a week before sending them out to the estates have all had beneficial results which are most encouraging. The reduction in death-rate in Negri Sembilan is particularly noticeable and Dr. Delmege deserves credit for what he has done there. Dysentery is diminished and ankylostomiasis though not a disease which appears to cause a great deal of acute illness yet it is recognized as a fairly constant infection amongst Indian labourers and much more attention is paid to it than formerly. Malaria is the great drawback but, as already reported, measures are being taken to combat this. It is more probable that the Indian suffers rather severely from it because his constitution has been somewhat undermined by the harbouring of worms as well as inadequate nourishment. Better feeding, which is now generally understood to be a matter which requires constant supervision on the part of employers, and eradication of worm disease enables the labourers to offer greater resistance to malaria, and the general improvement in health of estate labourers is probably largely due to these two factors, therefore when malaria is abolished an extremely satisfactory health condition may be confidently expected. In previous annual reports reference has been made to the importance of nourishing well-cooked food, especially for the Indian labourer. A book on "The Protein Element in Nutrition" by Major McCay, Professor of Physiology, Medical College, Calcutta, published in 1912, proves what can be gained by proper feeding and gives a clear description of suitable diets and their advantages—his work deals entirely with Indian people.

#### QUARANTINE STATION, PORT SWETTENHAM.

Sixty-two thousand one hundred and ninety-three immigrants passed through the camp at Port Swettenham during the year. The system of detention for a week for observation, vaccination and disinfection has continued to be very satisfactory in many ways and epidemics in this country have been prevented since the adoption of this arrangement.

#### TRAINING SUBORDINATE STAFF.

Much good work has been done by the Medical Officers in educating and training dressers. The standard is now a high one and the replies obtained at recent examinations show how careful the instruction has been. Many probationers have been admitted to the larger hospitals.

#### VENEREAL DISEASES.

The prevalence of these diseases should be a matter of deep concern. A visit to any of our hospitals is sufficient to convince any one of the universal incidence of them on a large scale; in fact, without any exaggeration, it might be said that without venereal disease and its results about 20 per cent. of present hospital accommodation would be unnecessary. Judging by the numbers of cases of long standing disease it does not appear that the old Enactments, now withdrawn, had much influence in preventing venereal diseases which are so prevalent, especially amongst Malays and Chinese. It may be possible to teach people how important and serious venereal diseases are and thus encourage them to seek efficient treatment early and save themselves from after results, but the best preventive measures which could be taken by Government are not designed yet. Many Chinese immigrants come here without their wives; it is a question whether encouragement of female immigration by the grant of special facilities for their transport might do some good.

#### OPERATIONS.

Messrs. V. Pal and S. Supramaniam, Assistant Surgeons at Batu Gajah, published interesting notes of a rare case of splenic abscess.

Seven hundred and thirty-two major and 2,757 minor operations were performed during the year at the various hospitals :

			Major.	Minor.
Perak	...	...	291	1,444
Selangor	...	...	247	813
Negri Sembilan	...	...	189	477
Pahang	...	...	5	23
		Total	<u>732</u>	<u>2,757</u>

#### VETERINARY.

##### RINDERPEST.

Only one outbreak occurred during the year in Selangor at Port Swettenham Quarantine Station amongst a consignment of 60 Siam bullocks which arrived from Singapore. There were in all eight cases, all of which recovered. One hundred contact animals were inoculated and no further spread occurred.

In Negri Sembilan five outbreaks occurred during the year at Chimpul Estate, Jelebu Road, 4th mile, Seremban; and at Ulu Bendul 41 animals were attacked out of which 21 died. Two hundred and thirteen animals were inoculated with anti-rinderpest serum.

No cases occurred in Pahang during the year—this is very satisfactory when compared with the serious outbreak last year, when 1,542 buffaloes died from rinderpest.

##### FOOT-AND-MOUTH DISEASE.

This disease was very prevalent in Perak during the year, though of a very mild type; there were a total of 457 cases of which 351 recovered.

In Selangor, with the exception of September when there were no cases, foot-and-mouth disease has been prevalent in a mild form throughout the year, the number varying from 855 in May to six in August.

In Negri Sembilan there were 845 cases with 28 deaths. Several outbreaks occurred in Pahang; so far this disease has been confined to the ulu side of Pahang.

##### SURRA.

There were nine cases of surra in Perak during the year.

##### QUARANTINE STATIONS.

Four thousand four hundred and thirty-three cattle were imported into Perak North through the different quarantine stations—viz., Port Weld, Parit Buntar, Upper Perak and Selama.

*Port Swettenham.*—Eight thousand eight hundred and two cattle were quarantined in this station, 91 of which died from various causes. The port was closed to all arrivals of cattle from July to September owing to the outbreak of rinderpest.

*Bukit Sentul.*—One thousand two hundred and eighty-eight cattle were quarantined here, and 142 cases of foot-and-mouth disease were treated at this station.

*Kuala Kubu.*—This station was very little used, only 28 cattle being quarantined here.

## PROSECUTIONS.

Six hundred and fifty-eight charges were brought before the Court for cruelty to animals and breaches of quarantine regulations, and fines imposed amounted to \$5,355.50.

## METEOROLOGY.

The mean temperature of the air for Taiping and Batu Gajah was  $81.50^{\circ}$  and  $81^{\circ}$ , respectively.

The highest temperature recorded at Taiping was 94° in the months of February and June to October.

The lowest mean temperature was 79° at Gopeng, Tapah and Lenggong.

The highest rainfall was at Selama with 230.15 inches as against 168.10 inches in 1912. Taiping came next with 195.74 inches as against 163.96 inches in 1912, and Tapah third with 179.04 inches.

The lowest rainfall at Grit, Lenggong and Kuala Kangsar was 80.69 inches, 80.67 inches, and 82.11 inches, respectively.

SELANGOR.

Highest temperature 97°; lowest 61°.

### Rainfall :

Kuala Kubu ... ... ... ... ... 123.22 inches  
 Kuala Selangor ... ... ... ... ... 66.79 "

## NEGRI SEMBILAN.

Highest temperature 94°; lowest 67°.

### Rainfall :

## PAHANG.

Highest temperature 96°; lowest 55°.

### Rainfall :

Sungei Tembeling ... ... ... ... ... 147.34 inches  
 Temerloh ... ... ... ... ... 77.73 "

VACCINATION.

	Perak	Selangor	Negri Sembilan	Pahang	Total	
Perak	...	...	...	...	...	38,707
Selangor	...	...	...	...	...	64,459
Negri Sembilan	...	...	...	...	...	5,854
Pahang	...	...	...	...	...	8,609
					Total	117,629

## STAFF.

It is with regret that I have to record the retirement from the service of Dr. G. D. Freer, Senior Medical Officer, Selangor, Negri Sembilan and Pahang, owing to ill-health.

Assistant Surgeon D. B. Perera also retired after 29 years' satisfactory service.

Dr. W. B. Orme was seconded for service to British North Borneo from 1st March, 1913.

Dr. A. A. Woods on his return from leave took up his new appointment as Health Officer, Lower Perak.

Dr. H. G. Holdbrook was transferred from the Colonial Service to the Federated Malay States, on promotion.

Doctors W. S. Coffey, W. M. Chambers, H. J. C. Grene and V. T. W. Eagles were appointed Medical Officers, Grade III.

Dr. J. H. C. Grene returned to England on the 27th December, 1913.

Doctors E. M. Layman, L. S. McLean and S. O'Flynn were appointed Lady Medical Officers and assumed duties during the middle of the year, the two former being stationed at Kuala Kangsar, and Miss S. O'Flynn at Kuala Lumpur.

A Veterinary Surgeon, Mr. H. G. Simpson, was appointed to Pahang during the year under review and assumed duty on 16th January, 1913, making Kuantan his head-quarters.

Nurses B. M. Dray, J. Thompson, E. Clarke, J. P. Morrissey and Miss Horsley were appointed during the year.

The following officers were absent on leave :

Dr. S. C. G. Fox, Senior Medical Officer, Perak ;  
 Dr. P. N. Gerrard, Medical Officer, Kuala Kangsar ;  
 Dr. W. P. Meldrum, Medical Officer, Seremban ;  
 Dr. W. S. Milne, Medical Officer, General Hospital, Kuala Lumpur ;  
 Dr. D. M. Ford, Medical Officer, Ipoh ;  
 Dr. P. H. Hennessy, Medical Officer, Kuala Pilah ;  
 Dr. E. A. Smith, Medical Officer, District Hospital, Kuala Lumpur ;  
 Dr. J. A. McIlroy, Medical Officer ;  
 Mr. Symonds, Veterinary Surgeon, Negri Sembilan.

#### BUILDINGS.

The following are the more important hospital buildings erected or altered during the year:

*General Hospital, Kuala Lumpur*—Quarters for six Nurse Probationers.

*District Hospital, Kuala Lumpur*—Lowering floor of five wards.

*European Hospital, Kuala Lumpur*—Ward for lunatics ; and New Nurses' quarters.

*Seremban*—New female ward for 40 beds, with two beds partitioned for maternity cases ;

Quarters for House Surgeon ;  
 European ward ;  
 Mortuary for European ward ;  
 Third class ward (clerks), 20 beds.

*Coast*—Female ward, 20 beds, Port Dickson ;

Infectious diseases ward at Port Dickson Hospital.

*Jelebu*—Malay ward, eight beds ;

Removal of mosquito gauze and substitution of expanded metal in wards.

*Tampin*—Married dressers' quarters ;

Two single quarters ;  
 Infectious diseases ward ;  
 New female ward, 20 beds.

*Kuala Pilah*—Twenty-bed ward with bath-room, examination room for females ;

Two dressers' quarters ;

Two attendants' quarters.

#### EXPENDITURE.

The total expenditure of the department, under Personal Emoluments, Other Charges, and Special Expenditure, amounted to \$1,763,307.52.

The following reports and returns are attached :

- (1) Report on Institute for Medical Research ;
- (2) Malaria Advisory Board Report ;
- (3) Return of Diseases, 1913.

CHARLES LANE SANSOM,

*Principal Medical Officer, F.M.S.*

REPORT ON THE INSTITUTE FOR MEDICAL RESEARCH  
FOR THE YEAR 1913.

UNPOLISHED RICE AND THE PREVENTION OF BERI-BERI.

Since the publication of our completed report on the etiology of beri-beri in 1912, various communications have been published by investigators who have sought to isolate from rice polishings the substance or substances which are of value in the prevention of beri-beri.

We found that by the extraction of polishings with acidulated alcohol a preparation was obtained which was effective in preventing the occurrence of polyneuritis in fowls fed on polished rice and of curing that disease in these animals. It is to extracts prepared by this method or similar ones, for an effective extract can also be prepared by means of acidulated water, that physiological chemists have devoted their efforts.

In this domain much work has been done by Funk who tested the value of the various substances which he isolated on pigeons suffering from polyneuritis induced by the consumption of polished rice. To a curative substance prepared by him he assigned the name "Vitamine," and gave it a formula calculated from the results of a single analysis; this formula he subsequently amended. As the molecular weights are unknown and as in the case of complex substances from the results of a combustion several formulae can usually be worked out, it is obvious that the formulae cannot be accepted without question. Moreover, from the variety of formulae he has given it is suggested that the substances were impure and, but for the fact that he has reduced the volume of the material in which the active substance or substances are contained, a proprietary name might quite as reasonably have been applied to the curative fraction isolated by us and known to be a mixture of substances. Indeed Tsuzuki has applied the name "Anti beri-berin" to the moist, black, sticky residue obtained on evaporation of the alcoholic extract.

Reasonable allowances for the magnitude and difficulties of the task confronting physiological chemists must be made, but the methods employed in the work require improvement; those now in use are crude and are sources of errors because of the incomplete separations they effect and because of the decomposition they so constantly produce. It may well be that the substance or substances which prevent beri-beri are elusive bodies and may never be isolated in a state of purity, but these problems in no way concern the physician or administrator whose work deals with the prevention and cure of beri-beri.

The fact that the continuous consumption of polished rice as the staple of diet gives rise to beri-beri in man rests on quite other testimony than that derived from experiments on fowls and pigeons and the fact is equally well established that when rice-eaters substitute unpolished rice for polished rice the disease does not occur.

Further valuable confirmatory evidence has recently been obtained from the results of the expedition conducted by Dr. Wollaston and Mr. Kloss into the interior of Dutch New Guinea where they had as their objective the exploration of the Snow Mountains.

The task which confronted them was, as both of them well knew, a formidable and an arduous one. Previous experience had shown them that the occurrence of beri-beri among them meant failure, thus the Goodfellow expedition of 1909-1911, undertaken to explore the Snow Mountains, was decimated by disease, and Dr. Wollaston, the Medical Officer to that expedition, has recorded that "in the six months from the beginning of June to the end of November, thirty-nine men showed definite signs of beri-beri and seven deaths were directly attributable to this cause."

The staple of diet was polished rice.

A similar fate befell all previously recorded expeditions into that country save the one conducted by Moszkowski and in which unpolished rice was used, but as his expedition only numbered ten men the results were inconclusive.

Convinced therefore that the work of the expedition could not be accomplished if their camp-followers and guard were fed on polished rice, Dr. Wollaston and Mr. Kloss decided that only unpolished rice should be used.

Here another difficulty confronted them. The only variety of unpolished rice which can be purchased in the Malay Peninsula in the open market is that known as parboiled rice. To that variety of rice the natives of India who immigrate to this country are accustomed and it is preferred by them. It has, however, an objectionable odour and appearance; irritating properties have been ascribed to it and it has even been thought to predispose to dysentery and the like diseases. Parboiled rice can be prepared free from these objectionable properties, but the manufacturers will not do so and abundant practical experience has shown that the use of parboiled rice is not the solution of the problem of beri-beri prevention.

Braddon held that parboiled rice was a preventive of beri-beri because it had been "cured," and that white rice was harmful because of some poisonous substance contained in it. The brilliant results obtained by the use of parboiled rice in the Government institutions of Malaya confirmed the accuracy of his view that such rice was a preventive of

beri-beri, but when we proved that white rice was harmful because by the process of polishing the sub-pericarpal layers were removed and that parboiled rice was only a variety of unpolished rice, the problem was entirely altered and the prevention of beri-beri was established on a rational basis.

Chinese, Malays, Javanese and the like may, when deprived of their liberty in prison, be compelled to partake of parboiled rice, but on regaining their liberty they will not continue its use. If on the other hand an ordinary unpolished rice or "kampong" rice were in use in such places, a demand would be created for that rice, which would then become available commercially. In this way some real progress might be recorded towards the eradication of a preventable disease. Fortunately in Java, where the use of parboiled rice is unknown, Dr. Wollaston and Mr. Kloss were able to obtain a supply of unpolished rice adequate for the needs of their expedition. In addition, acting on the suggestion of the writers, they took with them as an additional safe-guard a supply of our remedial agent, the use of which we have advocated in the prevention and cure of beri-beri.

The expedition consisted of 204 natives of the Malayan Archipelago, who were rice-eaters, together with two Europeans and four Eurasians.

They left Batavia about the end of August, 1912, and reached Dutch New Guinea in the middle of September. After reaching the coast, the explorers constructed canoes and ascended the Utakwa river. They went as far as they could go by water, the journey taking two days. They then proceeded overland by stages, each stage occupying three days. Depôts had to be constructed at each stage, an undertaking of considerable magnitude which occupied much time.

Four and a half months after they had arrived at the coast they reached the Snow Mountains, and then commenced their return journey to the coast which was reached in two months.

The expedition was in all of seven months' duration and, despite the laborious nature of the work, among the 204 rice-eating natives no single case of beri-beri occurred. The general health conditions of the expedition are reported to have been excellent.

The daily ration issued to the natives was as follows :

Rice	...	...	...	...	...	...	...	700	grms.
Fish or meat on alternate days	...	...	...	...	...	...	150	"	
Kachang idju	...	...	...	...	...	...	200	"	
Javanese sugar	...	...	...	...	...	...	50	"	
Coffee	...	...	...	...	...	...	20	"	
Tea	...	...	...	...	...	...	5	"	
Salt occasionally	...	...	...	...	...	...	20	"	

Two varieties of unpolished rice were used, one with a red pericarp during the first five months and one with a silvery pericarp during the last two months. Neither rice could be considered satisfactory from the cosmetic standpoint. In the case of the red variety only a partial attempt had been made to remove the pericarp and in the case of the silvery variety no attempt had been made to remove this valueless layer of the grain.

Despite the appearance no objections were raised by the natives to the use of these rices, but steps ought to be taken to induce manufacturers to remove the pericarp, and so improve the appearance of the grain.

In this connexion attention must again be directed to the valueless character of this structure. In previous reports the evidence has been furnished on which this statement is based, but writers, with but one or two notable exceptions, refer to the pericarp as the structure whose removal makes the rice harmful, whereas, in fact, it is the removal of the sub-pericarpal layers which is attended with this undesirable result. No real progress in the application of preventive measures can be made until there is available commercially an unpolished rice from which the pericarp has been removed.

Samples of both the rices used were analysed here with the following results :

	Red variety,				Silvery variety,			
	per cent.				per cent.			
Protein	...	...	...	...	...	9·22	...	9·41
Fat	...	...	...	...	...	1·14	...	2·10
Carbohydrate	...	...	...	...	...	78·64	...	76·57
Ash	...	...	...	...	...	1·06	...	1·50
Moisture	...	...	...	...	...	9·94	...	10·42
P <sub>2</sub> O <sub>5</sub> in Ash	...	...	...	...	...	0·54	...	0·79

It has been consistently advocated that a rice which yields not less than 0·4 per cent. of phosphorus pentoxide may safely be regarded as a harmless one and both of these rices are considerably over this standard, but only in the red variety did any of the grains show a partial removal of the sub-pericarpal layers and in the silvery variety the grain had only been deprived of its husk.

Had the enterprise of manufacturers so far progressed as to remove the pericarp and embryos from these grains, the results would have been equally satisfactory as regards the prevention of disease, the analysis would still have yielded results in accordance with the standard of safety and the cosmetic appearance of the food-stuff would have been greatly improved.

No fresh fish or meat was available during the expedition but only salt fish and dried, spiced beef.

Based on the standards we have previously adopted the ration was ample and the scientific findings are thus in complete accordance with the actual facts.

The results of this expedition as regards beri-beri are in striking contrast with those which obtained in all previous large expeditions into Dutch New Guinea and, taken in conjunction with the observations and experiments previously recorded by us, the absence of beri-beri on this occasion can only be explained in one way—that is, the absence of polished rice from the diet.

In 1909, we demonstrated :

1. That beri-beri as it exists in the Malay Peninsula is caused by the continuous consumption, as the staple of diet, of rice from which all or the greater part of the sub-pericarpal layers has been removed by the process of polishing.
2. That a satisfactory measure of the degree of polishing to which a rice has been subjected is the estimation of its total phosphorus in terms of phosphorus pentoxide.
3. That a rice which yields less than 0·4 per cent. of phosphorus pentoxide cannot safely be permitted to form the staple of a diet in man.

The evidence now submitted is a complete confirmation of the accuracy of these statements which, as we have repeatedly affirmed, were the logical deductions derived from systematic research.

Recently writers from Southern Nigeria and Brazil have disputed the accuracy of these conclusions, but we are unaware of any systematic observations having been carried out in these countries which would permit of a decided statement being made. When these are made it will be essential to determine that the disease known to them as beri-beri is the same as the disease which is known by that name here. After all, beri-beri is only a form of polyneuritis and students of this disease know that not only forms of polyneuritis of different origin have been called beri-beri, but that diseases of which polyneuritis may not be a prominent feature such as "Epidemic dropsy," "Ceylon beri-beri" and the like have been included under this name.

We have shown the mode of operation of the factors concerned in the etiology of beri-beri as it occurs in the Malay Peninsula. The painstaking researches of Hight and his colleagues have proved that the disease is of similar origin in Siam. Whilst the work of Strong and Cromwell has furnished similar evidence for the Philippine Islands. In the Netherlands India these results are in complete accordance with those obtained by the very able Dutch investigators.

There is then in the countries mentioned an endemic and epidemic disease which presents certain clinical features, and is known to clinicians in these countries as beri-beri. For the occurrence of that disease an explanation has been given. The disease can be prevented and, as we have shown elsewhere, may be cured. But, remembering the old adage that "prevention is better than cure," it is necessary to consider the practical application of preventive measures.

While fully appreciating the work of the scientists who seek to advance our knowledge on this subject we must be practical and attempt to reduce, if not abolish, the heavy toll which is yearly exacted by this disease.

The determination of exact knowledge is arrived at by processes of abstraction and elimination. In the practical application of that knowledge the disturbing factors have to be reincorporated and it is undoubtedly the magnitude of this task which has appalled administrators. But we are unable to convince ourselves that the difficulties are insurmountable. Political and commercial interests have too long been allowed to control the situation. Though such interests cannot be ignored they should not be given undue prominence in the consideration of preventive measures. Resolutions on the subject have been passed on two occasions by the Far Eastern Association of Tropical Medicine, and a resolution in almost identical terms was passed at the recent International Congress of Medicine. These pious expressions of opinion by learned societies in solemn conclave are likely to be and, in point of fact, have been without effect.

We have consistently advocated the preparation of an unpolished rice—that is, a rice from which the husk and the pericarp have been removed and which shall yield not less than 0·4 per cent. of phosphorus pentoxide. Such a rice can be and has been produced in Siam, but in the absence of a demand for it its preparation was not continued. The Governments of the countries concerned can create such a demand by making its use compulsory in all gaols and public institutions. In the Malay Peninsula that form of

unpolished rice known as parboiled rice is used in, practically, all such places, but, for the reasons we have mentioned, the use of that rice cannot be extended among the people and an unobjectionable, palatable, unpolished rice must be substituted.

A clause in Government contracts requiring the delivery of an unpolished rice conforming to the standard would give opportunity for observing how such a standard worked in practice, and aid in popularizing a safe and wholesome food-stuff among the people. No one believes that the introduction of such a measure would be accompanied by the immediate disappearance of beri-beri, but it is the only way in which progress in its prevention seems possible and it would bring such prevention within the sphere of practical politics.

In striking contrast with the brilliant results of the Wollaston-Kloss expedition are the disastrous results of an expedition undertaken in 1913 to the mountain called Gunong Tahan where the creation of a hill station for the Federated Malay States is contemplated. The expedition consisted of a survey party and comprised a surveyor with about fifty native assistants and labourers. These natives will not eat parboiled rice, but, for the reasons already stated, no other variety of unpolished rice was available commercially. They were, therefore, obliged to consume polished rice and an outbreak of beri-beri occurred.

Dr. Grijns, Director of the Geneeskundig Laboratorium, Weltevreden, informs us that by the use of unpolished rice the inhabitants of the Island of Billiton have ceased to suffer from beri-beri, and the troops in Batavia and Buitenzorg are now given unpolished rice with equally satisfactory results. Recently the use of unpolished rice has been extended to the miners on the Island of Banka, and Dr. Grijns considers it is only a matter of time until beri-beri shall cease to occur there.

#### THE CURE OF BERI-BERI.

In the annual report presented for 1912, experimental evidence was given in favour of a remedial agent which had proved of value in the cure of *Polyneuritis gallinarum*. It was proposed to extend the use of that preparation to patients suffering from beri-beri and to determine, if possible, its usefulness in this connexion.

It is a simple matter to put forward a remedy for disease and to assert that it is of value, but it is desired to ascertain by observation if the remedy possesses a real value and if so to establish its use on a rational basis. For that purpose conditions are required which are now non-existent and apparently unattainable. The work cannot therefore be carried out.

Some evidence in favour of the value of the remedial agent has been obtained from the Principal Medical Officer, Sarawak, who reports that "it undoubtedly does great good in certain cases," and that is all that can reasonably be expected of any cure for beri-beri. Unfortunately, we were able only to furnish him with a limited quantity of the remedy, and are unable to comply with his requests for further supplies, as also with similar requests which have reached us from other sources.

#### LEPROSY.

##### CULTIVATION EXPERIMENTS.

In the annual report for 1912 details were given of the experiments which had been carried out with a view to the cultivation of the *Bacillus lepræ*. During the year now under review further experiments were undertaken and other varieties of culture media employed.

In respect of the method by which material is obtained from cases of leprosy it has been found practicable to omit the use of iodine as a skin disinfectant. At first it was believed that the use of iodine was necessary in order to exclude contaminating micro-organisms, but the consistent failure of our efforts to cultivate the leprosy bacillus led us to consider the possibility, albeit a remote one, that the iodine might be in some way responsible for our failures and it was found that portions of subcutaneous tissue free from contamination could be obtained when no disinfectant for the skin was employed.

For the purpose of inoculating the tubes of media, the nodules were either transferred direct or emulsified in sterile salt-solution.

##### EXPERIMENTS WITH BLOOD-MEDIA.

The method of preparing these media was detailed in the annual report for 1912. Tubes of these media inoculated with leper material and incubated at 37°C. have now been under observation for two years and no culture of the *Bacillus lepræ* has been obtained.

##### FURTHER EXPERIMENTS WITH SERUM-AGAR.

It is a common experience that parasitic organisms when first induced to lead a saprophytic existence do not grow profusely, but that on repeated subcultivation luxuriant cultures are eventually obtained.

In view of the possibility of this being true of the leprosy bacillus the following experiment was carried out:

From a nodule situated in the left scapular region of a case of nodular leprosy (Case No. 25) a portion was excised and from it ten tubes of + 10 nutrient agar mixed with an equal quantity of human serum were inoculated. Each tube received a portion which varied

in size from a millet seed to a rice-grain. The tissue swarmed with leprosy bacilli. The inoculated tubes were incubated at 37°C. and from each tube the nodule was removed after intervals varying from seven to ten days and reinoculated on a fresh tube of the medium. The process of subculture was repeated regularly for three months. The maximum number of subcultures prepared from one nodule was eleven and in all upwards of a hundred tubes were inoculated. Not one of them became contaminated and not one of them showed a macroscopic growth. Persistence but not proliferation was invariably noted.

#### EXPERIMENTS WITH SERUM+STERILE AGAR.

In these experiments it was designed to substitute for the nutrient agar a medium of the following composition:

Powdered agar	...	...	...	...	...	...	40 grammes
Distilled water	...	...	...	...	...	...	1,000 c.c.

The mixture was dissolved in the autoclave and clarified with egg-albumen in the ordinary way. Tubes were then prepared each containing 5 c.c. of the medium and to each tube was added an equal quantity of human serum in the manner previously described.

From a nodule situated in the right lumbar region of a case of nodular leprosy (Case No. 35) a portion was excised and divided into pieces about the size of a rice-grain. Five tubes of the serum-agar were inoculated with these nodules. From a nodule situated just below and internal to the angle of the right scapula of a case of nodular leprosy (Case No. 36) a portion was excised and with it six tubes of the serum-agar were inoculated as in the previous case.

The inoculated tubes were incubated at 37°C. for three months. None of them became contaminated and a culture of the *Bacillus leprae* was not obtained.

#### EXPERIMENTS WITH ENGLISH PROOF-AGAR.

With this medium luxuriant growths of various fungi can be obtained.

Five tubes were inoculated with pieces of leper tissue obtained from Case No. 35 and five tubes were inoculated with similar pieces obtained from case No. 36.

The tubes were incubated for three months at 37°C. None of them have become contaminated and no culture was obtained.

#### EXPERIMENTS WITH CLEGG'S MEDIUM.

In his first communication, Clegg claimed to have grown the leprosy bacillus in symbiosis with amoebæ, a culture of which had been obtained from a case of dysentery.

Attempts made here to cultivate amoebæ have been uniformly unsuccessful and support the view of investigators who state that the pathogenic amoebæ have not been cultivated on artificial media.

In his second communication, Clegg states that he employed cultures of amoebæ obtained from water. By the methods he describes, a culture of amoebæ was prepared from water contained in a tank in the Institute and grown in pure culture with the vibrio of cholera.

Following exactly the procedure employed by him, twenty tubes of his medium were inoculated with the mixed culture of amoebæ and cholera vibrios. The inoculated tubes were incubated for twenty-four hours at 37°C. and then inoculated with lepromatous material.

From a nodule on the upper part of the left ear of Case No. 37 a portion was excised and emulsified with salt-solution. The emulsion contained leprosy bacilli in great abundance and from it five of the tubes were inoculated, one of the tubes receiving a small piece of the tissue which had not been properly emulsified. A second portion of the nodule was excised, cut into pieces the size of rice-grains and five of the tubes were inoculated with the fragments. From a nodule on the upper part of the left ear of Case No. 38 a portion was excised and emulsified with salt-solution. The emulsion contained leprosy bacilli in great abundance and from it five of the tubes were inoculated. From the same nodule a second portion was excised, cut into pieces the size of rice-grains and the remaining five tubes inoculated.

The twenty inoculated tubes were then incubated for one week at 37°C. On the expiry of that period reinoculations were made from each tube on to fresh tubes of Clegg's medium. The tubes, which had been inoculated with nodules of tissue, had the nodules removed to the fresh tubes along with a loopful of the amoebæ cholera culture. From the tubes inoculated with emulsion a loopful of the mixture of organisms was removed and inoculated on the fresh tubes. Smears were then prepared from each of the old cultures, stained and examined.

The procedure was repeated once a week for six weeks.

#### EXAMINATION OF ORIGINAL CULTURES AFTER INCUBATION.

The cultures, which had been inoculated with nodules of tissue from Case No. 37, showed the presence of cholera bacilli, amoebæ and acid-fast bacilli, the latter showing no change in morphology.

The cultures, which had been inoculated with the emulsion prepared from Case No. 37, showed cholera bacilli, amoebæ and acid-fast bacilli; but the latter were not so numerous as in the cultures inoculated with nodules of tissue.

The cultures prepared from Case No. 38 gave exactly similar results.

#### EXAMINATION OF 1ST SUBCULTURES.

In the subcultures which had been prepared with nodules of tissue from Case No. 37, many acid-fast bacilli were found. In two of them the bacilli were present in enormous numbers.

In two of the subcultures which had been inoculated with emulsion prepared from Case No. 37, acid-fast bacilli were not found, in one they were extremely scanty, in one a few scattered bacilli were observed, and in one acid-fast bacilli were quite numerous, mostly in clumps. The latter tube was the one previously referred to which had been inoculated with a nodule of tissue as well as with emulsion.

In the subcultures which had been prepared with nodules of tissue from Case No. 38, acid-fast bacilli were plentiful in each of the five tubes.

In the subcultures which had been prepared with emulsion from Case No. 38, acid-fast bacilli could be found only by a prolonged search, the bacilli were scattered, from two to five being found in a smear.

#### EXAMINATION OF 2ND SUBCULTURES.

In order to facilitate reference to these and subsequent cultures, each tube was numbered.

In the subcultures which had been prepared with nodules from Case No. 37 the results were:

1. Acid-fast bacilli were present but not very numerous. There were plenty of amoebæ both as vegetative forms and as cysts. Cholera bacilli present.
2. A few scattered acid-fast bacilli were found. There were plenty of both forms of amoebæ. Cholera bacilli present.
3. Acid-fast bacilli present, but not very numerous. There were a few of both kinds of amoebæ. Cholera bacilli present.
4. Acid-fast bacilli were scanty. Amoebæ and cholera bacilli scanty.
5. Acid-fast bacilli scanty. Both forms of amoebæ and cholera bacilli were present in moderate numbers.

In the subcultures which had been prepared from emulsion-cultures from Case No. 37 the results were:

1. No acid-fast bacilli were found.
2. Acid-fast bacilli were very numerous, but this is the culture which had a nodule of leper tissue.
3. No acid-fast bacilli were found.
4. No acid-fast bacilli were found.
5. No acid-fast bacilli were found.

There were numerous vegetative forms of amoebæ and cholera bacilli present in each film.

In the subcultures which had been prepared with nodules from Case No. 38 the results were:

1. Acid-fast bacilli present but not numerous, some scattered and a few in clumps. Cysts of amoebæ present but no vegetative forms.
2. Acid-fast bacilli present, but not numerous, chiefly small globi. Cysts of amoebæ numerous and a few vegetative forms.
3. A few acid-fast bacilli present. Both forms of amoebæ numerous.
4. A few acid-fast bacilli present. Both forms of amoebæ numerous.
5. A few acid-fast bacilli present. Both forms of amoebæ present but scanty.

In the subcultures which had been prepared from emulsion-cultures from Case No. 38 the results were:

1. No acid-fast bacilli present. Both forms of amoebæ abundant.
2. Two unaltered acid-fast bacilli found. Cysts of amoebæ numerous.
3. No acid-fast bacilli present. Both forms of amoebæ abundant.
4. No acid-fast bacilli present. A few cysts of amoebæ but no vegetative forms.
5. No acid-fast bacilli present. Both forms of amoebæ abundant.

## EXAMINATION OF 3RD SUBCULTURES.

In the subcultures which had been prepared with the nodules from Case No. 37 the results were :

1. Acid-fast bacilli numerous in small clumps. Both forms of amoebae were plentiful and cholera bacilli were fairly numerous.
2. Acid-fast bacilli numerous in small clumps. Both forms of amoebae were plentiful and cholera bacilli were fairly numerous.
3. Acid-fast bacilli present but not very plentiful. Both forms of amoebae present, the vegetative form being very numerous. Cholera bacilli fairly abundant.
4. Acid-fast bacilli few and scattered. Both forms of amoebae present and cholera bacilli fairly numerous.
5. Acid-fast bacilli few and scattered. Both forms of amoebae present and cholera bacilli fairly numerous.

In the subcultures which had been prepared from the emulsion-subcultures (Case No. 37) the results were :

1. No acid-fast bacilli present. Both forms of amoebae were present and the cholera bacilli were scanty.
2. Acid-fast bacilli were fairly numerous, small clumps. Both forms of amoebae were present and cholera bacilli were very scanty.
3. No acid-fast bacilli were present. Both forms of amoebae were present and cholera bacilli were very plentiful.
4. No acid-fast bacilli were present. Both forms of amoebae were present and cholera bacilli were scanty.
5. No acid-fast bacilli were present. Both forms of amoebae were present and cholera bacilli were scanty.

In the subcultures which had been prepared with the nodules from Case No. 38 the results were :

1. Acid-fast bacilli present, scattered and a few small clumps. Both forms of amoebae present.
2. Acid-fast bacilli present, scattered and a few small clumps. Both forms of amoebae present.
3. Only two small clumps of acid-fast bacilli found. Both forms of amoebae present and cholera bacilli very numerous.
4. Scattered acid-fast bacilli present and a few small clumps. Both forms of amoebae present. Cholera bacilli scanty.
5. Scattered acid-fast bacilli present and a few small clumps. Both forms of amoebae and cholera bacilli scanty.

In the subcultures which had been prepared from the emulsion-subcultures (Case No. 38) the results were :

1. Acid-fast bacilli absent. Both forms of amoebae present and cholera bacilli very numerous.
2. Acid-fast bacilli absent. Both forms of amoebae present and cholera bacilli very numerous.
3. Acid-fast bacilli absent. Both forms of amoebae present, vegetative forms and cholera bacilli scanty.
4. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli scanty.
5. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli scanty.

## EXAMINATION OF 4TH SUBCULTURES.

In the subcultures which had been prepared with the nodules from Case No. 37 the results were :

1. Acid-fast bacilli present as numerous small clumps and few scattered bacilli. Amoebae both forms present. Cholera bacilli few.
2. Acid-fast bacilli as in 1 but less numerous. Amoebae both forms present. Cholera bacilli few.
3. Acid-fast bacilli present, a few small clumps. Cysts of amoebae numerous, vegetative forms scanty. Cholera bacilli very few.
4. Acid-fast bacilli present, a few small clumps. Both forms of amoebae present. Cholera bacilli fairly numerous.
5. A few scattered acid-fast bacilli present. Both forms of amoebae present but vegetative forms scanty. Cholera bacilli very few.

In the subcultures which had been prepared from the emulsion-subcultures (Case No. 37) the results were :

1. Acid-fast bacilli absent. Cysts of amœbæ present but no vegetative forms. Cholera bacilli scanty.
2. A few small clumps of acid-fast bacilli. Both forms of amœbæ present. Cholera bacilli few.
3. Acid-fast bacilli absent. Both forms of amœbæ numerous. Cholera bacilli numerous.
4. Acid-fast bacilli absent. Cysts of amœbæ numerous but vegetative forms absent. Cholera bacilli few.
5. Acid-fast bacilli absent. Both forms of amœbæ numerous. Cholera bacilli very few.

In the subcultures which had been prepared with the nodules from Case No. 38 the results were :

1. Acid-fast bacilli very scanty. Cysts of amœbæ present but vegetative forms absent. Cholera bacilli very few.
2. A few clumps of acid-fast bacilli present. Both forms of amœbæ present but vegetative forms few. Cholera bacilli very few.
3. A few acid-fast bacilli present. Cysts of amœbæ present but vegetative forms absent. Cholera bacilli plentiful.
4. Acid-fast bacilli present, both clumps and scattered cysts of amœbæ present but vegetative forms absent. Cholera bacilli very few.
5. Acid-fast bacilli present, both clumps and scattered. Both forms of amœbæ present but vegetative forms scanty. Cholera bacilli very few.

In the subcultures which had been prepared from the emulsion-subcultures (Case No. 38) the results were :

1. Acid-fast bacilli absent. Both forms of amœbæ present but vegetative forms not numerous. Cholera bacilli very few.
2. Acid-fast bacilli absent. Both forms of amœbæ present but vegetative forms few. Cholera bacilli very few.
3. Acid-fast bacilli absent. Both forms of amœbæ present but vegetative forms few. Cholera bacilli very few.
4. Acid-fast bacilli absent. Both forms of amœbæ present. Cholera bacilli few.
5. Acid-fast bacilli absent. Both forms of amœbæ present. Cholera bacilli few.

#### EXAMINATION OF 5TH SUBCULTURES.

In the subcultures which had been prepared with the nodules from Case No. 37 the results were :

1. Acid-fast bacilli present, a few small clumps and scattered bacilli. Both forms of amœbæ present. Cholera bacilli plentiful.
2. Acid-fast bacilli present, a few small clumps and scattered bacilli. Both forms of amœbæ numerous. Cholera bacilli very plentiful.
3. A few scattered acid-fast bacilli present. Both forms of amœbæ present but vegetative forms scanty. Cholera bacilli very plentiful.
4. A very few small clumps of acid-fast bacilli present. Both forms of amœbæ present. Cholera bacilli very plentiful.
5. A very few small clumps of acid-fast bacilli present. Both forms of amœbæ present. Cholera bacilli very plentiful.

In the subcultures which had been prepared from the emulsion-subcultures (Case No. 37) the results were :

1. Acid-fast bacilli absent. Both forms of amœbæ present but vegetative forms scanty. Cholera bacilli very plentiful.
2. Acid-fast bacilli present, a few small clumps. Both forms of amœbæ plentiful. Cholera bacilli very numerous.
3. Acid-fast bacilli absent. Both forms of amœbæ numerous. Cholera bacilli very numerous.
4. Acid-fast bacilli absent. Both forms of amœbæ present. Cholera bacilli present.
5. Acid-fast bacilli absent. Both forms of amœbæ present. Cholera bacilli very numerous.

In the subcultures which had been prepared from the nodules from Case No. 38 the results were :

1. Acid-fast bacilli present in fairly numerous clumps, one very large globus. Both forms of amœbæ very numerous. Cholera bacilli numerous.
2. Acid-fast bacilli present, a few small clumps. Both forms of amœbæ numerous. Cholera bacilli very numerous.

3. Acid-fast bacilli present, numerous clumps and scattered bacilli. Both forms of amoebae present. Cholera bacilli present.
4. Acid-fast bacilli present, a few clumps and scattered bacilli. Both forms of amoebae present. Cholera bacilli scanty.
5. Acid-fast bacilli present, a few scattered small clumps. Both forms of amoebae present. Cholera bacilli very numerous.

In the subcultures which were prepared from the emulsion-subcultures (Case No. 38) the results were :

1. Acid-fast bacilli absent. Both forms of amoebae present, vegetative forms very numerous. Cholera bacilli very numerous.
2. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli present.
3. Acid-fast bacilli absent. Both forms of amoebae present, vegetative forms very numerous. Cholera bacilli numerous.
4. Acid-fast bacilli absent. Both forms of amoebae numerous. Cholera bacilli numerous.
5. Acid-fast bacilli absent. Both forms of amoebae numerous. Cholera bacilli numerous.

#### EXAMINATION OF 6TH SUBCULTURES.

In the subcultures which were prepared with the nodules from Case No. 37 the results were :

1. Acid-fast bacilli present, numerous large clumps. Both forms of amoebae numerous. Cholera bacilli present.
2. Acid-fast bacilli present, numerous clumps. Both forms of amoebae present but vegetative forms few. Cholera bacilli present.
3. Acid-fast bacilli present, a few small clumps. Both forms of amoebae present but motile forms few. Cholera bacilli plentiful.
4. Acid-fast bacilli present, clumps and scattered bacilli. Both forms of amoebae present, cysts plentiful. Cholera bacilli present.
5. A few acid-fast bacilli present. Both forms of amoebae present. Cholera bacilli present.

In the subcultures which had been prepared from emulsion-subcultures (Case No. 37) the results were :

1. Acid-fast bacilli absent, only amoebae cysts present. Cholera bacilli few.
2. A few acid-fast bacilli present. Both forms of amoebae present but vegetative forms few. Cholera bacilli scanty.
3. Acid-fast bacilli absent. Both forms of amoebae present, cysts numerous. Cholera bacilli very numerous.
4. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli present.
5. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli present.

In the subcultures which had been prepared with nodules from Case No. 38 the results were :

1. Acid-fast bacilli present, a few small scattered clumps. Both forms of amoebae present. Cholera bacilli present.
2. Acid-fast bacilli present, a few small scattered clumps. Both forms of amoebae present. Cholera bacilli present.
3. Acid-fast bacilli present, two or three small groups, only amoebae cysts present. Cholera bacilli very numerous.
4. Acid-fast bacilli present, a very few small clumps. Both forms of amoebae present but vegetative forms scanty. Cholera bacilli present.
5. Acid-fast bacilli present; a very few small clumps. A few amoebae cysts present. Cholera bacilli scanty.

In the subcultures prepared from the emulsion-subcultures the results were :

1. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli present.
2. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli present.
3. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli present.
4. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli present.
5. Acid-fast bacilli absent. Both forms of amoebae present. Cholera bacilli present.

The subcultures in this series in which acid-fast bacilli were found—that is, those prepared with nodules of tissue, were heated for half an hour at 60° C. Clegg states that by so doing the amoebae and cholera bacilli are killed but that the leprosy bacilli are unaffected. Subcultures were prepared from the heated cultures and incubated for one

week at 37° C. No growth of acid-fast bacilli was obtained but there was some proliferation of the amoebæ. Thus by following in detail the directions given by Clegg we have failed to obtain a culture of the leprosy bacillus. As has been observed in every one of our experiments, there was persistence but no evidence of proliferation.

The results are shown in the following table :

	2nd sub-cultures.	3rd sub-cultures.	4th sub-cultures.	5th sub-cultures.	6th sub-cultures.	
Case No. 37 ... Nodules of leper tissue	1. +	+	+	+	+	On these tubes (2) there was a nodule of leper tissue
	2. +	+	+	+	+	
	3. +	+	+	+	+	
	4. +	+	+	+	+	
	5. +	+	+	+	+	
Case No. 37 ... Emulsion of leper tissue	1. —	—	—	—	—	On these tubes (2) there was a nodule of leper tissue
	2. + +	+	+	+	+	
	3. —	—	—	—	—	
	4. —	—	—	—	—	
	5. —	—	—	—	—	
Case No. 38 ... Nodules of leper tissue	1. +	+	+	+	+	
	2. +	+	+	+	+	
	3. +	+	+	+	+	
	4. +	+	+	+	+	
	5. +	+	+	+	+	
Case No. 38 ... Emulsion of leper tissue	1. —	—	—	—	—	
	2. +	—	—	—	—	
	3. —	—	—	—	—	
	4. —	—	—	—	—	
	5. —	—	—	—	—	

#### EXPERIMENTS WITH CARREL'S MEDIUM.

Carrel, in a series of papers published in the *Journal of Experimental Medicine*, has described the technique by which the cultivation of tissues *in vitro* may be accomplished. Connective tissue, he states, can be successfully cultivated and as the leprosy bacilli with which we are working is contained in connective tissue, it was considered possible that by this procedure a culture of the *Bacillus lepræ* might be obtained.

The leper tissue was obtained on the 9th September, 1913, from a nodule on the upper part of the left ear of a case of nodular leprosy (Case No. 39). Smears, prepared from a portion of this tissue, showed the presence of enormous numbers of leprosy bacilli. The tissue was cut into small pieces. Two dishes were inoculated direct with these small pieces and a third dish was inoculated with a suspension of them in Ringer's fluid. The dishes were of the type devised by Gabritschewski and the medium was human plasma diluted with two-fifths its volume of sterile distilled water. The peripheral portion of the lower plate received sterile distilled water and the plates were sealed with vaseline. Incubation was carried out at 38° C. Carrel has stated that the life of a tissue *in vitro* is very short; he has devised methods by which this life can be prolonged and these methods we have employed.

After incubation it was noted that each nodule was surrounded by a hyaline area which contrasted sharply with the turbid coagulated plasma. On examination under a low power (the only one possible on account of the thickness of the dish-covers), there was no evidence of outgrowths from the nodules. The hyaline areas were caused by liquefaction of the plasma.

On the 13th September the nodules were removed from the Gabritschewski's dishes to plates containing Ringer's fluid and placed in the ice-box.

The liquefied areas were not apparently contaminated, at least smears prepared from these areas did not show the presence of contaminating micro-organisms. The liquefaction must therefore be attributed to the nodules of tissue, but whether due to the tissue or to the acid-fast bacilli it is impossible to say.

When the nodules had been for one and a quarter hours in Ringer's fluid at a temperature of 0° C. they were reinoculated on to dilute plasma spread on Gabritschewski's dishes and again incubated at 38° C. After incubation no hyaline areas were observed round the nodules and there was no apparent liquefaction of the medium.

On the 18th September the nodules were again transferred to Ringer's fluid and washed in it for one hour at 0° C., after which they were reinoculated on to dilute plasma and incubated at 38° C. On incubation, the three plates showed minute whitish

spots and it was suspected that contamination had occurred. On this occasion one of the nodules was reserved for microscopical examination. It was fixed by means of 10 per cent. formalin in normal salt-solution and imbedded in paraffin.

In sections stained by the Ziehl-Neelsen method and counterstained with methylene blue, the nodule appeared as an elongated piece of degenerated tissue, measuring 0.9 m.m. by 0.3 m.m., attached to a layer of coagulated plasma about 0.2 m.m. in thickness. The several elements which composed the piece of tissue were not differentiated by staining; the whole appeared as a hyaline structure devoid of nuclei and honeycombed with large sinusoid spaces. In some parts of thicker sections the spaces were packed full with acid-fast bacilli which suggested that these spaces represented the sites originally occupied by globi and that these had become broken up. Acid-fast bacilli were scattered in great profusion throughout the tissue, they did not appear to differ from the bacilli found in fresh leprous tissue, save that, perhaps, the beading was more pronounced. There was no evidence of tissue proliferation nor of proliferation of the acid-fast bacilli and there were no contaminating micro-organisms.

On the 24th September the nodules were removed and washed in Ringer's fluid for one hour and twenty minutes at 0° C. Films were then prepared from the whitish spots and no micro-organisms were found. After washing the nodules were reinoculated on dilute plasma and incubated as before.

On the 29th September the nodules were washed for two and a half hours and then reinoculated.

On the 4th October the nodules on two of the plates were washed and reinoculated. The nodules on the third plate were allowed to remain undisturbed. On the 8th and the 15th October the nodules on the two plates were washed and reinoculated. From the latter date onwards the nodules on all three plates were not disturbed and incubation was continued. The cellular elements having entirely disappeared from the tissue there appeared to be no advantage to be gained in respect of these structures by washing and reinoculation at short intervals, and it only remained to determine if plasma employed in this way was a suitable medium for the growth of the leprosy bacilli of which there was abundance remaining in the degenerate tissues. For that purpose it was considered best to leave the plates undisturbed, but at the close of the year no evidence was obtained that proliferation of the acid-fast bacilli had occurred.

More recently Carrel has stated that, if the pieces of connective tissue, which it is desired to cultivate, are transferred to fresh plasma at intervals of twenty-four or forty-eight hours, washing in Ringer's fluid is unnecessary. Experiments were carried out on these lines, leper tissue was cut into small pieces and inoculated on dilute human plasma in Gabritschewski's dishes. In one series the nodules were transferred to fresh plates every twenty-four hours and in the other transference was effected every forty-eight hours. The cells of the connective tissue suffered the same fate as these in the previous experiments and a culture of the *Bacillus leprae* was not obtained.

Carrel lays stress on the importance of embryonic juices as stimulants to the growth of the connective tissues, but we were not in a position to obtain human embryonic juices. On the other hand he does not state that human plasma obtained from adults is inimical to the growths of connective tissue and the cells of the connective tissue at the time of removal from the lepers on microscopical examination did not present appearances consistent with the belief that they were other than living cells. It is difficult to reconcile our failures with his brilliant results. If symbiosis with living cells is necessary for the proliferation of the leprosy bacillus then the methods we have employed must necessarily fail. Our previous experiments have shown that diluted and undiluted human serum are unsuitable media for the growth of the leprosy bacillus, our present experiments show that human plasma is equally unsuitable.

#### EXPERIMENTS WITH ASCITIC AGAR.

Nutrient agar containing two per cent. of agar and having a reaction + 10 was prepared, also a similar nutrient agar with a reaction—5. The media were filled into tubes each containing about 5 c.c. The tubes of media were sterilized in the ordinary way and when cooled to a temperature of 60° C. each tube received a volume of ascitic fluid equal to that of the nutrient agar. The contents of each tube were carefully mixed and placed in a water-bath at 60° C.

Six tubes of + 10 ascitic agar and six tubes of —5 ascitic agar were each inoculated with a portion of leper tissue which had been obtained from a non-ulcerating case (No. 40) of that disease. No time was lost between the removal of the tissue and its transference to the tubes. The inoculated tubes were immediately afterwards placed in a beaker of water at 60° C. and the whole transferred to a Bulloch's anærobic apparatus. The air was thoroughly exhausted for two hours, hydrogen was then passed into the apparatus. The tubes then received a layer of sterile liquid paraffin and were returned to the anærobic apparatus. The air was once more exhausted and replaced by hydrogen. The process was completed in the usual way and the tubes were incubated at 37.5° C.

It was aimed at obtaining complete anaerobiosis and the fact that the pyro-soda solution remained unchanged after two months showed that this result had been achieved, but a culture of the leprosy bacillus was not obtained.

A similar experiment was performed but with material obtained from another case (No. 41) of the disease and a similar result was obtained.

Material has now been obtained from forty-one non-ulcerating cases of leprosy and nearly a thousand inoculations have been made on a large variety of media. The results have been uniformly negative.

#### EXPERIMENTS ON ANIMALS.

Forty-five animals have been employed in connection with these transmission experiments. The consideration of these will be facilitated by their arrangement in groups.

The leper material was invariably obtained from non-ulcerating cases of the disease in accordance with the procedure described under the cultivation experiments.

#### RABBITS.

##### 1.—*Intra-ocular Inoculations.*

Eighteen rabbits have been dealt with in this way. In each case the right eye was selected and the nodule of tissue was placed in the anterior chamber. Thirteen of the rabbits each received nodules of leper tissue rich in leprosy bacilli, three of the rabbits received nodules of leper tissue rich in leprosy bacilli but the nodules had been heated for twenty minutes at a temperature of 120° C., and two of the rabbits received nodules of healthy subcutaneous tissue free from contaminating organisms.

**A. With Unheated Leper Tissue:** Of the thirteen rabbits inoculated with fresh unheated leper tissue, eight remained alive at the close of the year. Of these two have now been under observation for more than twelve months, four for nine months, and two for six months. All of them are apparently in perfect health and there is no evidence that transmission of the disease has been effected. As regards the five that are dead: Case No. 13 was observed to have a fungating growth at the site of incision thirty days after inoculation. As nothing was to be gained by a continuance of this condition the animal was killed and examined. Apart from the condition of the eye, the animal was apparently healthy. A detailed examination of the right globe showed that the scar of the incision had given way and that the iris had prolapsed. The remains of the nodule were represented by a quantity of degenerate tissue situated near to the cut end of Descemet's membrane and containing large and small masses of acid-fast bacilli. Case No. 19 died forty days after inoculation and the coccidiosis present was sufficient to account for death. The examination of the right globe showed that the nodule of leper tissue had become converted into a small mass of degenerate tissue which stained badly and had lost most of its cell-nuclei. The leprosy bacilli persisted in great masses but were confined to the remains of the nodule.

There was no infiltration around the remains of the nodule which had caused very little inflammatory reaction. Case No. 6 died ninety-six days after inoculation. At no time did it appear to be ill. Post-mortem the stomach was found to be much distended and contained a solid mass of food-stuffs coated with tenacious mucus: apart from this there was nothing to account for death. The right globe on examination showed that the remains of the leper-nodule had become incorporated in the anterior part of the iris. By strands of fibrous tissue and blood-vessels derived from the iris, the nodule had become subdivided into irregular spaces which contained the globular remains of cells packed with acid-fast bacilli and scattered iris pigment. Acid-fast bacilli were found only in the situation occupied by the remains of the nodule.

Case No. 11 died one hundred and eleven days after inoculation. The animal appeared always to be in good health. On the day of its death it had been taken from the cage for the daily examination. It suddenly became convulsed, it was placed on the ground and ran away. Almost immediately afterwards it was seen to be dying. It died within ten minutes. Post-mortem a hard fleshy tumour was found at the site of the pancreas. From the lower part of the tumour there extended downwards a firm mass which on incision was found to contain a large clot of recent origin—this was apparently the cause of death. In the right eye a staphyloma had formed at the site of the incision and on microscopical examination it was found that the remains of the original nodule had worked its way into the staphyloma and then become embedded in the cornea, in front of Descemet's membrane where it lay surrounded by a mass of small cells. In the meshes formed by the remains of the leper nodule there were vast numbers of acid-fast bacilli, but not elsewhere.

Case No. 7 died two hundred and forty-three days after inoculation. Fat necrosis was found in the pancreas and mesentery. In the liver and spleen there were numerous areas of focal necrosis, the cause of these lesions was not discovered. The right globe showed a condition of buphthalmos, the cornea was opaque and projected as a large staphyloma. On microscopical examination it was found that the nodule of leper tissue had behaved in a

similar manner to that described in Case No. 11. Acid-fast bacilli were abundant in the necrotic leper tissue, but they were less acid-fast than the bacilli in fresh leper tissue. Acid-fast bacilli were also found in comparatively small numbers among the large mono-nuclear cells surrounding the remains of the leper tissue and a few were found between the layers of the cornea up to a distance of 7 m.m. from the nodule. No acid-fast bacilli were found at a greater distance than this from the nodule and none were found in other parts of the body. There were no contaminating micro-organisms present in any of the tissues.

**B. With Heated Leper Tissue:** Of the three rabbits inoculated with sterilized nodules of leper tissue two remained alive at the close of the year. Over six months had then elapsed since the material was inoculated and the effect on the eyes did not appear to differ from that in other eyes into which unheated leper tissue had been introduced. The third rabbit (Case No. 22) died seventy-four days after the inoculation. About the fourth week a moist eczema appeared on the skin of the abdomen and a week later the left hind leg became paralysed, a similar disease affected many of our stock of rabbits. The paralysis and eczema persisted and the animal died in a very much emaciated condition. Microscopical examination of the right globe showed that the nodule of tissue had behaved in the same way as the nodules of unheated leper tissue, and that the bacilli retained both their form and their acid-fastness.

**C. With Normal Subcutaneous Tissue:** The two rabbits, which had been inoculated with nodules of healthy subcutaneous tissue, were alive at the close of the year—that is, more than six months since the date of inoculation. The ocular changes are similar to those observed in the rabbits inoculated with unheated and with heated nodules of leper tissue.

#### *Intra-peritoneal Injections.*

On the 9th September three rabbits each received an intra-peritoneal injection of 0.5 c.c. of an emulsion rich in leprosy bacilli and prepared from freshly excised nodules of leper tissue. Two remained alive and healthy at the close of the year. One (Case No. 33) died on the 15th November. It remained healthy and apparently normal until the 12th November when it refused food. No acid-fast bacilli or other organisms were found in the viscera. There was cloudy swelling of the liver and some degeneration of the central zones of the lobules. The cells lining the convoluted tubules of the kidney were swollen and indistinct and had lost many of their nuclei. The other viscera showed no pathological changes.

#### *Intra-testicular Injections.*

On the 9th September three rabbits each received an intra-testicular injection of 0.5 c.c. of an emulsion rich in leprosy bacilli and prepared from freshly excised nodules of leper tissue. All three of them were alive and healthy at the close of the year.

#### GUINEA-PIGS.

##### *Intra-ocular Inoculations.*

Three guinea-pigs, which had each received nodules of leper tissue in the anterior chamber of their right eyes, have been under observation for six months. There is nothing to indicate that they have become infected with leprosy.

##### *Intra-testicular Inoculations.*

Three guinea-pigs each had a nodule of leper tissue inserted in the *tunica vaginalis*. Six months later as nothing appeared to have happened each animal received an intra-testicular inoculation of 0.5 c.c. of an emulsion of fresh leper tissue rich in acid-fast bacilli. Three and a half months afterwards, the animals appeared perfectly healthy.

Three guinea-pigs each received an intra-testicular injection of an emulsion rich in leprosy bacilli and two months later as nothing had happened they received a further injection. Three and a half months later, the animals were in perfect health.

#### RATS.

Five wild rats have been inoculated with nodules of leper tissue. One, which had been inoculated at the root of the tail, died on the following day. The blood swarmed with trypanosomes.

Of three others similarly inoculated, one died after an interval of three and a half months, one died after six months and one died after nine months. The nodules of leper tissue had behaved in a manner similar to their behaviour in the eyes—that is, the cellular elements of the tissue had undergone disintegration, the bacilli persisted and were confined to the nodules.

One rat which had received a nodule of leper tissue in the scrotum was alive at the close of the year. It has been under observation for over nine months and its health does not appear to be impaired.

#### FOWLS.

Six full-grown cocks were selected on the 16th December. In the comb of each with the aid of a sharp scalpel a pocket was made and a nodule of leper tissue inserted. The wound in each case was closed with a silk-worm-gut suture and healed perfectly. At the close of the year there was nothing to note.

## MONKEYS.

So far only one of these has been made the subject of experiment. A female gibbon (*Hyalobates lar*) was inoculated with an emulsion of leper tissue in the supraorbital region. One month later it was reinoculated in the same region with a nodule of leper tissue and twenty-five days later it died of dysentery. Diffusion or proliferation of the leprosy bacilli was not observed. Gibbons do not do well in captivity, they are extremely liable to be attacked by dysentery with fatal results. It appears improbable that they will be of assistance in these researches and in future experiments it is proposed to use a more hardy type of monkey.

In this connexion a common monkey (*Macacus nemestrinus*) was procured. It was apparently in good health. It was not convenient then to perform the inoculation. After some weeks the animal developed paralysis of the lower extremities and weakness of the upper extremities. Trophic ulcers developed on both upper and lower extremities. It was fortunate that the animal had not been inoculated with leper material otherwise it might have been difficult to convince ourselves that the paralysis, etc., had not developed as a result of the inoculation.

Number of Experiment.	Animal.	Date of inoculation.	Site of inoculation.	Material inoculated.	Interval between removal from body and inoculation.	Patient's number.	Remarks.
1	Rabbit ...	27-12-12	Anterior chamber of right eye	Portion of Leproma	1 hour ...	24	
2	Gibbon F.	22-8-12	Supraorbital region	Emulsion of "juice expressed from erythematous patch	1 $\frac{1}{2}$ " ...	24	
3						20	
4	Wild rat ...	27-12-12	Root of tail ...	Portion of leproma...	1 $\frac{1}{2}$ hours ...	24	
5	Rabbit ...	7-3-13	" Anterior chamber of right eye	" "	24 hours ...	24	
6						28	
7	" ...	"	" "	"	1 $\frac{1}{2}$ hour ...	29	
8	" ...	"	" "	"	1 $\frac{1}{4}$ " ...	30	
9	" ...	"	" "	"	2 hours ...	30	
10	" ...	11-3-13	" "	"	1 $\frac{1}{4}$ " ...	31	
11	" ...	"	" "	"	1 $\frac{1}{2}$ " ...	31	
12	" ...	"	Anterior chamber of right eye	Portion of leproma...	2 hours ...	31	Died 11 a.m., 30-6-13
13	" ...	"	" "	"	2 " ...	31	Fungating growth noted at site of incision 10-4-13. Rabbit killed
14	Rat M. ...	"	Serotum	" "	2 $\frac{1}{2}$ " ...	31	
15	" F. ...	"	Root of tail	" "	2 $\frac{1}{2}$ " ...	31	
16	" F. ...	"	" "	"	3 " ...	31	
17	Guinea-pig M.	12-3-13	Serotum	" /	1 hour ...	32	Reinoculated 9-9-13 in left testicle with 0.5 c.c. of emulsion rich in leprosy bacilli from Case 39
18	" ...	"	Tunica vaginalis	"	1 " ...	32	Reinoculated 9-9-13 as in Case 17
19	Rabbit ...	"	Anterior chamber of right eye	"	1 $\frac{1}{2}$ hours ...	32	Died 21-4-13. Coccidiosis
20	Guinea-pig M.	"	Tunica vaginalis	"	1 $\frac{1}{2}$ " ...	32	Reinoculated 9-9-13 as in Case 17
21	Rabbit ...	24-6-13	Anterior chamber of right eye	"	3 " ...	33	
22	" ...	"	" "	Portion of leproma which had been heated 20 minutes at 120°	4 " ...	33	Died 6-9-13
23	" ...	"	Anterior chamber of right eye	Portion of leproma...	3 " ...	34	
24	" ...	"	" "	Portion of leproma which had been heated 20 minutes at 120°	4 " ...	34	
25	Guinea-pig M.	10-7-13	" "	Portion of leproma...	4 " ...	34	
26					1 hour ...	35	
27	" ...	"	" "	"	1 $\frac{1}{2}$ hours ...	35	
28	" ...	"	Left testicle "	"	3 " ...	35	
29	" ...	"	" "	Emulsion of leproma	2 " ...	36	Reinoculated 9-9-13 as in Case 17
30	" ...	"	" "	"	2 " ...	36	" "
31	Rabbit F.	9-9-13	Intra-peritoneal inoculation	1/2 c.c. of emulsion rich in leprosy bacilli	2 " ...	36	" "
32	Rabbit M.	"	" "	"	3 " ...	39	
33	" ...	"	" "	"	3 " ...	39	
34	" ...	"	" "	"	3 " ...	39	
35	" ...	"	Intra-testicular inoculation L	"	3 " ...	39	
36	" ...	"	" "	"	3 " ...	39	
37	Rabbit F.	18-9-13	Anterior chamber of right eye	Piece of normal subcutaneous tissue	3 " ...	39	
38	Rabbit M.	"	" "	"	1 hour ...		
39	Cock ...	16-12-13	Pocket made in comb	Portion of leproma...	1 $\frac{1}{2}$ " ...	42	Died 1-1-14 at 1.30 p.m.
40							
41	" ...	"	" "	"	1 $\frac{1}{2}$ " ...	42	
42	" ...	"	" "	"	1 $\frac{1}{2}$ " ...	42	
43	" ...	"	" "	"	1 $\frac{1}{2}$ " ...	42	
44	" ...	"	" "	"	1 $\frac{1}{2}$ " ...	42	
45	" ...	"	" "	"	1 $\frac{1}{2}$ " ...	42	

## ACID-FAST BACILLI IN THE CONJUNCTIVAL SACS OF RABBITS.

On 13th June, 1913, a rabbit, into whose eye a piece of leper tissue had been inoculated three months before, was observed to have a slight, tenacious, mucoid discharge from the inoculated eye. On examination of this discharge it was discovered to contain acid-fast bacilli. Two days later other rabbits, which had been inoculated with leper tissue, were examined and acid-fast bacilli were found in the eyes of five out of eight of them; not only in the inoculated, but also in the uninoculated eye. Six healthy rabbits were then taken from the enclosure in which the stock of animals is kept and smears were made from the contents of their conjunctival sacs, acid-fast organisms were found in all of them. On the following day an examination was made of three healthy rabbits which had never been in the enclosure, but had been kept in a separate cage; acid-fast bacilli were not found.

These acid-fast organisms produced no injurious effects upon the rabbits and their presence was a temporary phenomenon of short duration. On 21st June the organisms were found in two out of six rabbits taken from the enclosure. In one of those animals in which they were not found on this occasion, they had been abundant a week before. On 24th June five rabbits, in which acid-fast bacilli had been found ten days previously, were re-examined with the result that the organisms were found in only one of them. On 18th and 19th August fourteen rabbits from the enclosure and three, which had been isolated in cages, were examined with negative results. Subsequently all the rabbits, which had been inoculated with leper tissue, were re-examined, but no acid-fast organisms were found in any of them.

The acid-fast organisms found in the eyes of these rabbits were arranged in clumps and masses; a few scattered bacilli were present. Some of them were indistinguishable from leprosy bacilli, but, for the most part, they appeared to be shorter and stouter.

Attempts were made to obtain cultures of these organisms. On 16th June six rabbits were selected, in which acid-fast bacilli had been found in the conjunctival sacs. From each rabbit, a tube of nutrient agar and a tube of serum-agar were inoculated. The tubes were incubated at 37° C. No growth of acid-fast organisms was obtained.

On 18th June similar tubes were inoculated from the same six rabbits. The tubes inoculated from three of the rabbits were incubated at 37° C.; the tubes inoculated from the other three were kept at room temperature. No growth of acid-fast organisms was obtained.

On 21st June, six healthy rabbits were examined and acid-fast bacilli were found in two of them. Smears from the conjunctival sacs of each of these rabbits were made on nutrient agar and on serum-agar. The tubes were kept at room temperature. No growth of acid-fast organisms was obtained.

On 27th June a rabbit was selected in which acid-fast organisms were found in the conjunctival sac. Two tubes of nutrient agar and two of glycerine-agar were inoculated. One tube of each medium was incubated at 37° C. and the others were kept at room temperature. No growth of acid-fast organisms was obtained.

## PARASITOLOGY.

Dr. Stanton furnishes the following report:

Studies of the larval and pupal stages of *Anopheles*, *Stegomyia*, and other genera of mosquitoes have been continued. Specimens bred from ova laid by females in captivity have formed the basis of this study and it is hoped by this means to avoid those inaccuracies which are liable to result in the absence of such experimental work. The larval forms not hitherto described of the following species have thus been dealt with—*Anopheles tessellatus*, Theobald; *Anopheles kochi*, Donitz; *Ochlerotatus niveus*, Ludlow; *Rachionotomyia aranoides*, Theobald; *Taeniorhynchus (Culex) ager*, Giles; *Culex mimeticus*, Noe.

At the suggestion of the Director of the Imperial Bureau of Entomology data have been collected as to the distribution of the various species of *Stegomyia* in this and neighbouring countries. It is considered that this information will be of value in connection with any measures which it may be decided to undertake to prevent the spread of yellow fever to the Orient when the Panama Canal is opened to traffic.

For the purpose of this inquiry material has been obtained from the following countries in addition to the Federated Malay States: Sumatra, British North Borneo, Kelantan, Straits Settlements and Indo-China. In all of these countries near the sea-coast both *Stegomyia fasciata*, the known carrier of yellow fever, and *S. scutellaris* are found in abundance but inland only the latter species as a rule; in Kuala Lumpur, an inland town, *S. fasciata* is comparatively speaking a rare mosquito. These mosquitoes have been found breeding in most unusual situations, in one instance in an uncovered bottle of mucilage; this adaptability suggests that their eradication or effective diminution in numbers in these latitudes will be a difficult task.

Other species of *Stegomyia* such as *S. trilineata*, Theob. and the closely allied *Ochlerotatus niveus*, Ludl. have only a limited range of distribution in Malaya and are essentially jungle mosquitoes.

The larvæ of the two common species of *Stegomyia fasciata* and *scutellaris* have been studied in detail. It has been found that the characters usually given by authors for the differentiation of species of larvæ in the *Stegomyia* group are practically valueless for this purpose. In the mature larvæ of this group, as in *Anopheles*, the form and arrangement of the clypeal hairs and other hairs on the dorsum of the head afford a ready and reliable means of identifying the species.

The genus *Phlebotomus* (sand flies) members of which have been shown in India and elsewhere to be transmitting agents of dengue-like fevers has been found to be represented in Malaya by at least one species—namely, *Phlebotomus perturbans*, Meijere. This is the first record of *Phlebotomus* in the Malay Peninsula.

Collections of mosquitoes and other biting flies have been sent to workers in special groups at the King Institute, Madras, the London School of Tropical Medicine, the Imperial Bureau of Entomology, the British Museum and the United States National Museum. Several species new to science have been included in these collections.

#### ANOPHELES AND MALARIA IN THE ORIENTAL REGION.

Dr. Stanton has continued his researches on this subject and furnishes the following report :

Though the anopheles factor is only one in a complex of conditions which result in severe or epidemic malaria, it is happily one that is open to attack by public measures. It is of high importance therefore that we should be acquainted with the species of *Anopheles*, their relationship to man and to those parasites of man which they transmit.

This study has been much hampered by the uncertain state of nomenclature in the group. It has been found on the one hand that identical mosquitoes are known under different names in different countries and on the other hand that different mosquitoes are known under the same name. This question of accuracy or at least uniformity in nomenclature of species is of importance to the sanitarian for it is probable that the same or similar species will be found to have similar habits and habitat in whatever country they are found and so the knowledge gained of malaria-carrying species in one country can be turned to account in others.

Some attempt in the direction of this uniformity has already been made by Major James, I.M.S., and myself in regard to India and the Malay Peninsula and lately through the courtesy of Dr. Schuffner in regard to Sumatra and the Malay Peninsula. The inclusion of Indo-China, the Philippine Islands, Formosa, and other countries in a scheme for the systematic study of Oriental species of *Anopheles* would, I am convinced, do much to advance knowledge and thereby to increase the effectiveness of preventive measures against malaria.

In the record of *Anopheles* from the Malay Peninsula thirty-five species-names occur in the literature but not more than eighteen of these are of valid species which exist in that area. In the following lists I give : (I) the names of those Malayan species which are now regarded as valid ; (II) the species-names occurring in the literature which are regarded as synonyms ; (III) the names of those valid species which are believed to have been erroneously recorded from the Malay Peninsula.

#### I.—VALID SPECIES.

<i>Aitkeni</i> , James	<i>Leucosphyrus</i> , Donitz
<i>Albirostris</i> , Theobald	<i>Ludlowi</i> , Theobald
<i>Albotæniatus</i> „	<i>Maculatus</i> „
<i>Aurirostris</i> , Watson	<i>Rossi</i> , Giles
<i>Asiaticus</i> , Leicester	<i>Sinensis</i> , Wiedemann
<i>Barbirostris</i> , Van der Wulp	<i>Tessellatus</i> , Theobald
<i>Fuliginosus</i> , Giles	<i>Umbrosus</i> „
<i>Karwari</i> , James	<i>Watsoni</i> , Leicester
<i>Kochi</i> , Donitz	<i>Wellingtonianus</i> , Alcock.

#### II.—SYNONYMS.

<i>Elegans</i> , James	= <i>Leucosphyrus</i> , Donitz
<i>Fragilis</i> , Theobald	= <i>Aitkeni</i> , James
<i>Halli</i> , James	= <i>Kochi</i> , Donitz
<i>Leucophyrus</i> , Leicester	= <i>Leucosphyrus</i> , Donitz
<i>Minutus</i> , Theobald	= <i>Sinensis</i> , Wiedemann
<i>Nivipes</i> „	= <i>Fuliginosus</i> , Giles
<i>Ocellatus</i> „	= <i>Kochi</i> , Donitz
<i>Peditæniatus</i> , Leicester	= <i>Sinensis</i> , Wiedemann
<i>Separatus</i> „	= <i>Sinensis</i> „
<i>Treacherii</i> „	= <i>Aitkeni</i> , James
<i>Vanus</i> , Walker	= <i>Sinensis</i> , Wiedemann

## III.—ERRORS IN IDENTIFICATION.

*Listoni*, Liston for *Albirostris*, Theobald

*Punctulatus*, Donitz „ *Tessellatus* „

*Willmori*, James „ *Maculatus* „

A few words with reference to those species which are common to Sumatra and Malaya may not be inopportune. Professor Donitz was engaged in describing the anopheline fauna of Sumatra and Java at about the same time that Mr. Theobald was engaged on that of Malaya. The consequence was that many species now known to be identical were described under different names. English speaking workers in India and elsewhere have for the most part adopted the nomenclature of Mr. Theobald, in some cases neglecting the fact that Professor Donitz' descriptions were published first. I have recently had the opportunity of examining some of Donitz' preparations preserved in the British Museum and of comparing Malayan with Sumatran specimens.

I find for example that Donitz' *Anopheles kochi* is identical with the species known as *Christophersia halli* in India and which James and I found to be identical with Malayan specimens. Theobald considered that the peculiar position of the abdominal scale tufts in this species warranted the creation of a new species and a new genus for its reception. Donitz' description of *kochi* is however perfectly clear on this point. He notes that the scale tufts lie ventrally and diverge from the middle line. The correct name for this species is therefore *kochi*, Donitz. Similarly *elegans*, James, is identical with *leucosphyrus*, Donitz; *leucopus*, Donitz, and *nivipes*, Theobald, are identical with *fuliginosus*, Giles; *deceptor*, Donitz, with *tessellatus*, Theobald; while *aconitus*, Donitz, is very near if not identical with Theobald's *albirostris*.

## RECORDS OF MALARIA INFECTION IN ANOPHELES.

James enumerates the following species as proved carriers of malaria in India: *culicifacies*, Giles; *fuliginosus*, Giles; *listoni*, Liston; *maculipalpis*, James and Liston; *stephensi*, Liston. To this list must be added the species *willmori* found infected by Mrs. Adic in the Kangra valley.

Christophers states that in the Andamans *ludlowi* is the carrier of malignant malaria.

From Sumatra Schuffner (1902) reported that he has observed the development of malaria parasites in an anopheline species referred to by him as "Anopheles I" and which Eysell claims to be *rossi*. De Vogel (1910) also reports the successful infection of *rossi* bred from salt-water pools.

From Formosa, Miyajima and Kinoshita have recorded that *listoni* and *annulipes* are carriers of malignant malaria and *sinensis* of benign tertian. Tsuzuki found a species which he refers to as *A. formosensis* to be a carrier.

In the Federated Malay States, Leicester has reported negative results in feeding experiments with *rossi*, *sinensis* and *barbirostris*. Watson has recorded "*willmori*," *karwari* and "*umbrosus X*" as carriers; he notes that he found both zygotes and sporozoites in "*willmori*," but the details of observations or experiments with other species are not given. James and I have recorded natural and experimental infection in the species *albirostris*. I have found *maculatus*, *fuliginosus* and *sinensis* naturally infected and have observed the development of the parasites of malignant malaria in *albirostris*, *fuliginosus* and *maculatus*.

Having thus cleared the way by a statement of the recorded instances of malaria infection in Anopheles, the evidence on which the claims of authors are based may now be reviewed.

## THE LISTONI GROUP.

The three species *listoni*, *culicifacies* and *albirostris* may conveniently be taken together. The first two have been shown by several observers, Stephens and Christophers, James and others to be important agents in the spread of malaria in India. The species *listoni* is also stated to occur in Indo-China and Formosa, and in these countries also has been found to be a very dangerous species.

Major James and I reported at the 1912 meeting of the Far Eastern Association of Tropical Medicine that the parasites of malignant tertian malaria readily undergo development in the species *albirostris* and that we had found this species infected in nature.

Of 78 specimens of *albirostris* taken in nature three were found to be infected. Of 22 specimens fed on blood containing malignant tertian gametocytes, 9 were found infected. In one specimen which had fed several times, more than two hundred zygotes were counted. Zygotes developed up to full maturity but the completed cycle with sporozoites in the salivary gland was not observed. Major Lalor has reported finding sporozoites in the salivary glands of a specimen of *listoni* var *alboapicalis* in Burmah—this species is, I believe, *albirostris*.

Tsuzuki's *A. formosensis* which he found to be a carrier in Formosa is said by Donitz to be only a variety of his *aconitus*. As I have already said this species is probably identical with Malayan *albirostris*. *Albirostris* possesses the distinctive character of absence of flecking on the 3rd long vein which Donitz laid stress upon as diagnostic of his *aconitus* and in other features it closely corresponds to the latter species.

*Albirostris* has also been reported from Calcutta and the Andaman Islands under the name *brahmacharii*. I have also examined specimens taken in Burmah.

#### THE "NYSSORHYNCHUS" GROUP.

##### ANOPHELES FULIGINOSUS.

First incriminated as a malaria-carrier by Stephens and Christophers. Adie found sporozoites in the salivary glands of specimens taken in the Punjab.

It is a common species in the Malay Peninsula where it has been known as *nivipes*. Comparison of Malayan *nivipes* with Indian *fuliginosus* has shown that they are the same species. Christophers however prefers to regard the Andamans type as a variety of *fuliginosus*.

Its larvae are common in pools and lakes with weedy margins.

In my experiments with this species, of 23 specimens taken in nature one showed zygotes and of 10 fed on blood containing gametocytes of malignant tertian malaria, two developed zygotes.

##### ANOPHELES MACULATUS.

A common species in India and the Malay Peninsula, originally described from specimens taken in Hongkong. It occurs also in Sumatra and Formosa.

It has been redescribed by Leicester from the Malay States under the name *willmori*. *Maculatus* and *willmori* are however two distinct species. In examining the type specimens of the species *maculatus* in the British Museum I found that the male and female types were of two different species, the male only being of the species usually known to students of the Oriental group as *maculatus*. In this circumstance lies the explanation of the confusion which has existed regarding the nomenclature of this and closely allied forms.

It was proved to be a carrier by Watson in the Federated Malay States, who showed also that it was associated with severe malaria in hilly country.

In my experiments, of 32 specimens taken in nature and dissected, two were infected and of seven specimens fed on blood containing malignant tertian gametocytes one developed zygotes.

The species *maculipalpis*, *willmori*, and *stephensi* which also belong to the "Nyssorhynchus" group have been proved to be carriers in India. What relationship *annulipes* of Formosa bears to other Oriental species I have been unable to determine.

#### THE SPECIES *Umbrosus* AND *Sinensis*.

##### ANOPHELES UMBROSUS.

This species has been found infected in nature by Watson in the Federated Malay States, but the details of his observations have not been published. I am informed by Col. Alcock that *umbrosus* has also been found infected in Borneo. In my own experiments six dissections and five feeding experiments were negative.

##### ANOPHELES SINENSIS.

Tsuzuki has shown that this species, referred to by him as *A. jesaeensis* is a carrier of benign tertian malaria in Japan. Kinoshita also in Formosa found it to be a carrier of benign tertian and quartan but not of malignant tertian malaria.

In 87 dissections I found two specimens infected with full grown zygotes—the species of parasite could therefore not be determined. In 11 specimens fed on crescent containing blood none developed zygotes.

#### THE *Rossi* GROUP.

I come now to the consideration of a group of anopheles about which there has been much argument—the *rossi* group. The three types *rossi*, *indefinitus*, and *ludlowi* which are variously regarded by some as a single species, by others as one species and two varieties, and by others as three distinct species are obviously closely related. One or other of them is a common species in every country of the Oriental region. What part do they play in malaria transmission?

In India the work of many competent observers over a series of years warrants the conclusion that *rossi* as there defined is not a carrier. Bentley from his extensive investigation in Bombay concludes that this species is naturally refractory to malaria infection.

The commonest type of *rossi*-like anopheles in the Malay Peninsula is that species or variety known as *indefinatus*. It differs slightly from typical Indian *rossi* in the palpal markings. One hundred and fourteen dissections of the mid-gut and salivary glands of Malayan specimens taken in nature showed no infected individuals and of 22 specimens fed on blood containing numerous crescents none became infected. It seems improbable therefore that this variety of *rossi* is a carrier in the Malay Peninsula.

Eysell cites Kinoshita, Banks, De Vogel and Schuffner in support of his contention that *rossi* is an important agent in the transmission of malaria. His citation of Kinoshita is an error as *rossi* was not one of the species which that author found to carry malaria in Formosa. Banks experimented with the species *ludlowi*, though he afterwards concluded that this species was identical with *rossi*; his description has been held to suggest doubts as to the nature of the bodies which he believed to be malaria parasites. De Vogel says that he was able to infect only specimens which had bred from salt water. It is now known that *ludlowi* breeds by preference in such situations and it has been suggested that it was with this species that De Vogel dealt. Schuffner's Anopheles I, according to Eysell, identical with *vagus*, Donitz, and therefore with *rossi*; Giles.

Major Christophers working in the Andamans records finding two infected specimens of *ludlowi* out of 53 examined and from his study of the conditions there concludes that "the chief carrier of malaria in the settlement is *ludlowi*, a species which breeds in and about salt swamps."

It must be admitted that the evidence with regard to these *rossi*-like mosquitoes is very unsatisfactory and as they are common species everywhere in the Orient their relationship to malaria is deserving of further study.

In addition to the species dealt with above I have carried out experiments with the following species with negative results:

	Dissections.							Feeding experiments.	
<i>Karwari</i>	...	...	...	...	...	...	20	...	—
<i>Barbirostris</i>	...	...	...	...	...	...	16	...	8
<i>Kochi</i>	...	...	...	...	...	...	7	...	4

This survey of what is known of the distribution of Anopheles in the Oriental region and of their relationship to malaria reveals the fact that the most important agents in the spread of malignant malaria are that group of small brown anopheles which includes *listoni*, *culicifacies* and *albirostris*. These are hardy species, voracious blood suckers and intimate in their association with man. Next in general importance is the "Nyssorhynchus" group which comprises *maculatus*, *fuliginosus* and *stephensi*. The part played by such species as *ludlowi*, *sinensis*, and *umbrosus* is less clearly defined and seems to warrant further inquiry.

#### BLACKWATER FEVER.

Dr. Fletcher has continued his researches on this subject and furnishes the following report:

Eighteen cases of blackwater fever were reported during the year and, when it was possible, the cases were visited and the urine and blood examined. In addition to the above, four cases were reported in which the diagnosis was not confirmed. In two of these, the urine was ordinary febrile urine, containing neither blood nor albumen; the other two patients were suffering from gross lesions of the bladder with accompanying haematuria. During the year 1912 only two cases of true blackwater fever were investigated. The increase in the cases reported during 1913 is probably due, in part at least, to a circular issued in the previous year inviting medical men to notify cases of this disease.

**Nationality.**—Though there are but comparatively few Europeans in the country, they contributed a large proportion of the cases. Eight of the patients were Europeans, six were Indians, three Chinese and one Japanese. Doubtless some cases of blackwater in Asiatics escape observation; sometimes they are not recognized even in hospitals, for the urine is voided in the urinal attached to the ward or, if the patient be very ill, it is passed through a hole in the bed-board, into an iron bucket where its colour may be overlooked by the dresser in charge of the ward.

**Locality.**—Nine of the cases occurred in the State of Negri Sembilan, five in Selangor, three in Perak, and one in Pahang. All but four of the patients were employed on rubber estates and, in nearly every instance, the district in which the patient lived was notoriously malarious.

**Quinine.**—In three cases (Nos. 5, 6 and 18) the patients had taken no quinine for at least a week, before the onset of the attack of blackwater. All the patients were treated with quinine during the attack except two fatal cases; one of these was comatose and died soon after his admission to hospital, the other was given quinine by the mouth but never retained it. Three cases were treated with small doses of quinine and one died. Two were given fifteen grains a day and both recovered. Eleven patients were treated with large doses of quinine—that is to say, twenty grains or more every twenty-four hours, and, of these eleven patients, nine recovered.

Though it cannot be shown that the quinine administered in these cases, had any influence in cutting short the disease, it is quite evident that it did not have the effect of prolonging it. To take a specific instance: case No. 10 was in hospital undergoing treatment for malaria when the blackwater appeared, which it did three hours after an intra-muscular injection of ten grains of quinine. The injections were not discontinued or diminished; another dose of ten grains was given four hours after the appearance of the blackwater, twenty grains were injected during the course of the following day and, thereafter, thirty grains, a day, were given by the mouth. In this case the blackwater lasted for only twenty-four hours and, though quinine was continued for sometime after its disappearance, in doses amounting to thirty grains a day, there was no relapse. The patient was given quinine in large doses, before the attack, during the attack and throughout his convalescence. When these points are considered in conjunction with the fact, noted above, that three of the patients had not taken quinine before the attack came on, it appears most unlikely that quinine can be an important factor in the etiology of blackwater fever.

*Malaria.*—All the patients had suffered from malaria; nearly all of them had suffered severely. Most of them came from districts which were notoriously malarious. In every instance a fever, which the patients themselves considered to be malarial, preceded the attack of blackwater. The presence of pigment in the leucocytes and an increase in the number of the large mononuclear elements of the blood, afforded presumptive evidence of recent malaria. In four cases, in which the blood was examined less than twenty-four hours before the attack, the parasites of subtertian malaria were found in every instance. In one particularly mild case (No. 16), crescents and simple tertian parasites persisted, in the blood, throughout the attack of blackwater. In the other cases the parasites were destroyed, or disappeared, very soon after the onset of the disease.

*The Blood.*—The presence of subtertian parasites, in some cases, and the collateral evidence of malaria, provided by the increased proportion of the large mononuclear cells and the presence of intra-leucocytic pigment, have been mentioned already.

In five cases a few cubic centimetres of blood were withdrawn from one of the median veins of the forearm. In each instance, the serum and the citrated plasma were of a much darker colour than is the case with normal blood. In three of the five cases (Nos. 12, 13 and 15), the blood was obtained while the patient was still passing black urine. In one of them (No. 15), the serum and citrated plasma were tinged with red, and the colour of the serum matched a 0.25 per cent. solution of normal blood in distilled water. This was the only instance in which oxyhaemoglobin bands were seen in the serum. In this case, when the urine began to clear, the red tinge disappeared from the serum which then became yellow-coloured and no longer contained oxyhaemoglobin. In case No. 12 the serum was orange-coloured and contained methaemoglobin. In case No. 13 the citrated plasma was of a greenish-yellow colour, no haemoglobin bands could be seen on spectroscopic examination, but, when ammonium sulphide and caustic potash were added, the characteristic spectrum of haemochromogen appeared. In two other cases (Nos. 14 and 16), the blood was drawn off after the urine had become clear. No haemoglobin was present in either the serum or the citrated plasma.

*Urine.*—In all the cases, except two in which methaemoglobin was found alone, the urine passed during the attack contained oxyhaemoglobin; in four cases, this was mixed with methaemoglobin. The deposit, in the blackwater urine, consisted of blood-debris, chiefly in the form of minute, yellow globules, one or two microns in diameter, which gave the same staining reactions as red blood-corpuscles. In some cases needles of haematoidin were seen, mixed with the globules. Tubular casts were always present. These casts, which are commonly known as haemoglobin-casts, were of a brownish-yellow colour; they were composed of blood-debris and a few epithelial cells. In some cases the urine contained epithelial cells from the renal pelvis.

*Morbid Anatomy.*—It was possible to carry out an autopsy in only three of the fatal cases: in one of these the examination of the material obtained has not yet been completed. As in former cases, it was in the liver that the most striking changes were encountered. In this organ, there was a profound destruction of the liver cells around the hepatic veins. In the cells of the portal zones there was a dark pigment which contained iron in loose organic combination. In the central zones there were blocks of yellow, iron-free pigment.

Many of the kidney tubules contained casts, composed of yellow blood-debris. In these casts, and in the epithelium of the convoluted tubules, there were fine granules of brown pigment which contained iron. In all cases, dark brown pigment was found in the spleen, liver and kidneys.

#### EXPERIMENTS WITH THE SERUM AND CORPUSCLES FROM CASES OF BLACKWATER.

In three cases, experiments were undertaken to determine, firstly if the serum contained any antibodies which were specific for human corpuscles, and secondly if the corpuscles of these patients were more readily susceptible than normal corpuscles, to the action of human serum. Many normal human sera contain iso-agglutinins, some authors state that they may contain isolysins; moreover, in some healthy persons, the corpuscles appear to be especially susceptible to the action of the serum of other normal individuals.

The result of these experiments was negative: the serum from the peripheral blood of the cases of blackwater examined, contained no specific antibodies for other human corpuscles or for washed corpuscles from the same source as the serum; nor were the blackwater corpuscles more readily lysed or agglutinated, than normal corpuscles, by the action of normal serum. It appears most unlikely that an autolysin should be found in the serum of blackwater fever, for as soon as such an antibody passed into the circulation it would be anchored by the corpuscles in the blood stream.

The following are the details of these examinations:

(Case 14).—Blood was drawn from this patient on the third day of his illness, after the urine had become clear. Fresh normal human serum was added: (1) to normal human corpuscles; (2) to corpuscles from a case of subtertian malaria; (3) to corpuscles from this case of blackwater. The normal corpuscles and the malarial corpuscles were not agglutinated or lysed. The blackwater corpuscles were slightly agglutinated when 0.3 c.c. of fresh normal serum were added to 0.1 c.c. of a 20 per cent. emulsion of the corpuscles.

Serum, from this case of blackwater, did not agglutinate or lyse its own corpuscles; but it agglutinated normal corpuscles and malarial corpuscles. When, in addition to the blackwater serum, human complement was added, there was slight lysis in both cases. It was thought that the blackwater serum might contain a substance which had a selective action upon corpuscles containing malarial parasites. This was found not to be the case. Blackwater serum and complement were added to an emulsion of corpuscles many of which contained subtertian rings. After twenty-four hours, when about half the corpuscles had undergone lysis, slides were prepared from those which remained. The corpuscles containing parasites were, proportionately, as numerous as before.

(Case 15).—Blood was taken from this case on three occasions: (1) seventeen hours after the onset; (2) on the third day; (3) on the fifth day. When the first two samples were taken, haematuria was still present.

Serum.—Samples of serum, from these three specimens, were added to the following corpuscles: (A) corpuscles from a normal person; (B) corpuscles from a case of untreated severe subtertian malaria; (C) corpuscles from a patient with severe subtertian malaria, who had received thirty grains of quinine sulphate two hours before. None of the three samples of serum produced lysis or agglutination of any of the three samples of corpuscles, except in the case of serum (3) which caused slight agglutination of the corpuscles (C).

Corpuscles.—Emulsions of washed corpuscles prepared from the three specimens of blood drawn from this patient were added to: (a) serum from a normal individual; (b) serum from a case of untreated, severe, subtertian malaria; (c) serum from a patient with severe, subtertian malaria, who had received thirty grains of quinine sulphate, two hours before; (d) serum from a man with a wound on his foot. No lysis or agglutination occurred except where serum (d) was employed; this serum not only agglutinated the blackwater corpuscles, but also the corpuscles from all the other cases (A), (B) and (C).

(Case 16).—The serum derived from a sample of blood taken from this patient, on the day after the haemoglobinuria had ceased, was added to washed corpuscles, from a normal individual, with the result that the corpuscles were strongly agglutinated but not lysed. The serum from the same normal individual produced slight agglutination of the blackwater corpuscles.

#### EXPERIMENTS WITH WATERY EXTRACTS OF THE LIVER AND SPLEEN OF BLACKWATER CASES.

The profound destruction of the parenchyma of the liver which has been observed in the fatal cases of blackwater investigated here, suggested that the immediate cause of the blood-destruction might be found in this organ.

In two cases, an extract of the liver was made by passing pieces of the organs through a mincing machine and adding distilled water in the proportion of 99 c.c. to one gramme of minced liver, and allowing it to stand over night, in the ice-box, at 0° C. The next morning, the mixture was filtered, first through asbestos and, then, through a sterile Berkefeld filter. Sodium chloride to the amount of 0.8 per cent. was added to the filtrate. This extract was then added, in graduated quantities, to normal human corpuscles obtained from several sources and to corpuscles from a case of blackwater fever, but no lysis or agglutination occurred.

Experiments were also made with a watery extract of the spleen. One part of minced spleen was added to 99 parts of distilled water and kept for four days at 0° C. The mixture was then centrifuged and the supernatant fluid employed. In quantities of 0.2 c.c. this extract produced agglutination and partial lysis when added to 0.1 c.c. of 20 per cent. emulsions of normal corpuscles and of corpuscles from a case of malaria. When serum and corpuscles from the same case were mixed, before the extract was added, the serum inhibited the lysis of its own corpuscles.

No conclusions can be drawn from these experiments until control observations have been made and until other methods have been tried for making extracts of the organs.

The subjoined table, in which are set out the main features of the cases investigated, is followed by accounts of them in greater detail.

No.	Date.	Age.	Nationality.	Place.	Occupation.	Previous attack of blackwater.	History of malaria.	History of quinine.	Quinine immediately before attack.	Amount of urine.	Treatment.	Result.	Remarks.
1	26-2-13	35?	European	Seremban, Negri Sembilan	Rubber planter	...	Very frequent attacks	Took quinine irregularly	Had taken quinine	Rather scanty	Quinine in large doses	Urine cleared on 5th day.	
2	22-3-13	30	Do. ...	New Labu, Negri Sembilan	Do.	...	Do.	Took quinine when he had fever	Had taken quinine as usual	Do.	Recovered	Recovered on 4th day.	
3	4-4-13	20	Tamil ...	Tanjong Maim, Perak	Rubber estate cooly.	...	Twice during month of attack	Quinine, gr. v daily	Plentiful ...	Plentiful ...	Urine cleared on 3rd day.		
4	21-5-13	26	European	Seremban, Negri Sembilan	Rubber planter	...	Only once during three months previous to attack. Before that much fever	Took quinine irregularly	?	Scanty ...	Recovered	Recovered	
5	2-8-13	30	Do. ...	Gopeng, Perak	Tin miner	One, nine months before	Very frequent attacks	No quinine...	None...	Admitted unconscious and died soon afterwards	... Plentiful ...	Die ...	No quinine taken before the attack
6	7-8-13	32	Malaya-lum.	Raub, Pahang	Rubber planter	One, three years before	Only one attack in last three years. Frequent before	Took quinine irregularly	Do. ...	Do. ...	Quinine in large doses	Urine cleared on 4th day.	
7	8-8-13	42	Chinesc...	Seremban, Negri Sembilan	Do.	...	Very frequent attacks	Gr. xxx the day before the attack	Do. ...	Recovered	Recovered	Recovered	
8	6-9-13	37	Chinese...	Rembau, Negri Sembilan	Goldsmith	...	Frequent attacks	Gr. x shortly before the attack	?	Do.	Urine cleared on 6th day.		
9	19-9-13	30?	European	Kuala Selangor, Seremban, Negri Sembilan	Rubber planter	One, two years before	Do.	Quinine xv daily	Plentiful as usual	Plentiful ...	Quinine gr. xv daily		
10	21- 9-13	26	Chinese	Shop (carpenter). Living on rubber estate until six months before attack		...	Frequent attacks	Took quinine irregularly	Plentiful ...	Plentiful ...	Urine cleared in 24 hours.		

11	6-10-13	25	Ceylonese	Perhentian Tin-gi, Negri Sem- bilan	Railway clerk	...	Had malaria almost continu- ously for six months before the attack	Quinine phite gr. xxx on each of two days immedi- ately preceding the attack	Do.	Recovered ...	Subtertian malarial parasites were pre- sent in this patient's blood on the day on which he was attacked by black- water
12	14-10-13	15	Tamil	... Boungsar, Kuala Lumpur	School-boy. Living on Rubb er estate	...	Had suffered a good deal from subtertian ma- alaria	Took quinine when he had fever	B. a t h e r scanty	Quinine in small doses	Urine cleared on 3rd day. Recovered
13	20-10-13	27	European	Batu Tiga, Selangor	Rubber planter	...	Twelve attacks during preced- ing three months	Quinine sul- phite gr. xv daily	Gr. xv as usual	No qui- nine	Died 63 hours after com- mencement
14	30-10-13	33	Tamil	... Cheviot, Negri Sem- bilan	Planter's clerk	...	Occasional attacks	Took quinine when he had fever	Took gr. xx the day be- fore the attack	Q u i n i n e in large doses	Urine cleared after 48 hours. Re- covered
15	14-11-13	28	European	Kajang, Selangor	Rubber planter	...	Had simple tertian malaria four months before the attack; since then exception- ally free	Do.	Took gr. xxxv during 12 hours before the attack	Q u i n i n e in small doses	Urine cleared on the 5th day but patient died on 7th day
16	27-11-13	24	Eurasian	Siputeh, Perak	Do.	...	Very frequent attacks	Took quinine irregularly	Plentiful ...	Q u i n i n e in very small doses	Urine cleared in 24 hours. Recovered
17	27-11-13	33	Japanese	Sungei Gadut, Negri Sem- bilan	Living on rubber estate	...	Slight fever occa- sionally	Took quinine when she had fever	Took gr. x during 48 hours before the attack	Q u i n i n e in large doses	Died 57 hours after onset
18	26-11-13	40	Malaya- lum	Kuala Selangor, Selangor	Rubber estate	...	Had fever two months before the attack and two days before	Took quinine when he had fever	Gr. xv daily	Urine cleared in 48 hours and patient recovered	Had taken no quinine for at least a week before onset of blackwater. Sub- tertian rings found in the blood on the day before the on- set of blackwater

## CLINICAL DETAILS OF CASES.

## Case 1. February 26th, 1913.

A European, planter, aged 35, from Seremban in Negri Sembilan. He had been in the country for about twelve months. He had suffered much from fever and was in the habit of taking quinine and aspirin irregularly. When he was admitted to the Seremban Hospital, his urine was black and had been so for two days. His temperature was 102.5° F.; but no malarial parasites were found in his blood. He was treated with quinine, in the usual doses employed in the treatment of uncomplicated malaria, and he recovered.

When his urine was examined here, on the sixth day of his illness, the spectroscope showed no trace of haemoglobinuria, but the urine contained a little albumen and the yellow granular casts which are generally seen in cases of blackwater fever.

## Case 2. March 22nd, 1913.

A European, planter, aged about 30, from New Labu Estate in Negri Sembilan. He had lived for four years in the Federated Malay States and had suffered, during the whole of that period, from frequent attacks of malaria, for the cure of which it was his custom to take quinine and aspirin. On the third day of his last attack of fever, for which he was taking quinine as usual, his urine became black and he was admitted to hospital on the following day. His urine, which was the colour of porter, contained methaemoglobin and a few casts. No parasites were found in his blood. He was given quinine intra-muscularly and by the mouth. His urine became clear on the fourth day.

## Case 3. April 4th, 1913.

A Tamil, cooly, aged 20 years, from the Tanjong Malim Rubber Estate at Tanjong Malim in Perak.

This man had suffered twice from "fever" during the two months prior to his attack of blackwater. He was in the habit of taking five grains of quinine daily as a prophylactic.

When seen, he had been suffering from blackwater fever for two days. He was anaemic and jaundiced, and his spleen was enlarged. The urine, at this time, was the colour of claret; it contained a small amount of amorphous blood debris, uric-acid crystals and a little albumen. No casts were seen. The patient was passing a fair quantity of urine. Spectroscopic examination showed the presence of oxyhaemoglobin and a small quantity of methaemoglobin.

This patient was treated with bihydrochloride of quinine, three grains every three hours. The urine became clear on the third day and he recovered.

## Case 4. May 21st, 1913.

A European, planter, aged 26 years, from a rubber estate (Bute) in Negri Sembilan. He had suffered frequently from malaria for several years in Assam, in Johore and in Malacca, before he came to Negri Sembilan three months prior to his attack of blackwater fever. He was in the habit of taking quinine fairly regularly, and during the last three months, he had had only one attack of fever.

Five days before his urine was examined at this Institute, he had a rigor and, shortly afterwards, passed very dark urine. Two days later, when he was admitted to the Seremban Hospital, he was passing a small amount of bloody urine; he was very restless and vomited almost incessantly. Over his abdomen, shoulders and elbows there were dark, purpuric blotches. He was treated with intra-muscular injections of quinine and also received injections of normal saline solution and horse-serum. This case terminated fatally.

A spectroscopic examination of the urine demonstrated the presence of oxyhaemoglobin. The deposit was composed of blood-debris, bacteria and numerous desquamated cells.

No parasites were found in the blood-smears. The white cells were in the following proportions :

Polymorphonuclears	...	...	...	...	...	...	...	54
Small Lymphocytes	...	...	...	...	...	...	...	30
Large Mononuclears	...	...	...	...	...	...	...	14
Eosinophiles	...	...	...	...	...	...	...	1
Mast cells	...	...	...	...	...	...	...	1

## Case 5. August 2nd, 1913.

A European, miner, aged 30, from Gopeng in Perak. This patient had suffered a great deal from subtertian malaria and he had had a previous attack of blackwater eight months before. He was not in the habit of taking quinine and he had been suffering from fever for some time when he, suddenly, became unconscious while at work. On the following day he was admitted to Batu Gajah Hospital in a condition of delirium, and he died about twenty-four hours later. A sample of urine, taken on the day of his admission to hospital, was of a dark mahogany colour. It contained a small quantity of oxyhaemoglobin.

There was a copious deposit, consisting of blood-debris, haematoxin needles, "haemoglobin" casts, granular and fatty casts, and a few epithelial cells. The urine showed a cloud of albumen on boiling.

In a sample of urine taken on the following day, no haemoglobin bands could be detected by spectroscopic examination, and no blood-debris could be seen in the deposit which consisted, largely, of fatty and granular casts containing a few epithelial cells.

No parasites were found in the blood, which showed a moderate degree of poikilocytosis and the presence of a few nucleated red cells. A differential count of the white cells gave the following result:

Polymorphonuclears	...	...	...	...	...	...	...	51
Small Lymphocytes	...	...	...	...	...	...	...	32
Large Mononuclears	...	...	...	...	...	...	...	17
Eosinophiles	...	...	...	...	...	...	...	0

All the organs received for examination were in an advanced stage of putrefaction, so that sections, made from them, could not be stained for microscopical examination.

The liver showed a quantity of free iron in the centre of the trabeculae of the portal zones of the lobules. Towards the middle of the lobules, also in the centre of the trabeculae, there was pigment of a golden colour. There were abundant granules and lumps of malarial pigment in, and near, the walls of the capillaries. The liver was so much altered by post-mortem changes that little could be learned from stained sections. The central part of many of the lobules had undergone necrosis with fragmentation of the trabeculae.

The spleen-pulp was crowded with putrefactive organisms, the nuclei and cells had lost all power of differential staining and the histological structure of the organ had been destroyed by decomposition. Large blocks and fine granules of malarial pigment were present in abundance.

In the kidney, putrefaction had advanced too far for anything to be learned from sections of that organ.

#### Case 6. August 3rd, 1913.

A Malayalum, cooly, aged 32, from a rubber estate (Sungei Bulit) in Pahang. He had lived seven years in Pahang and before that, for three years, he was in Penang and Province Wellesley.

This man had suffered from blackwater fever three years before his present attack, when he was working on another estate (Cheroh). On that occasion his urine was black for ten days. Since that time he had been employed on a more healthy estate and had only once had fever. The first symptom of his present attack was the passing of black urine. Two hours later he had rigor and felt feverish. He had taken no quinine before he passed the black urine. On the following day, he was admitted into Raub Hospital. On the third day of his illness no malarial parasites were found in his blood, but the Medical Officer in charge of the case reports that he found them on the fourth and fifth days of the attack. Blood-smears, made on the evening of the fifth day and examined here, contained no parasites.

The white cells were in the following proportions :

Polymorphonuclears	...	...	...	...	...	...	...	50.0
Small Lymphocytes	...	...	...	...	...	...	...	31.5
Large Mononuclears	...	...	...	...	...	...	...	16.0
Eosinophiles	...	...	...	...	...	...	...	2.5

The urine became clear at the end of the fourth day. A specimen passed at 3 p.m. was the colour of porter and contained oxy-and methaemoglobin, haemoglobin casts and a few epithelial cells. When boiled, the specimen was almost solid with albumen. Urine passed five hours later contained a little less albumen and no blood could be recognized by spectroscopic examination. In a specimen passed at mid-night the amount of albumen was slightly reduced, granular casts and degenerate epithelial cells were present, but no blood.

This patient was treated with quinine; thirty grains a day by the mouth and he was given saline injections. He recovered.

#### Case 7. August 8th, 1913.

A Chinese cooly, aged 42, from a rubber estate (Gedoug Lalang) in Seremban. This man had lived for twenty years in the Malay States and, for some time, he had suffered from malaria almost continuously. He took quinine irregularly and, the day before his attack of blackwater began, he had taken thirty grains.

The urine and blood of this patient were examined on the first day of his attack. The urine was a dark port-wine colour; it contained oxyhaemoglobin, a little methaemoglobin and a deposit, which consisted of amorphous blood-debris and a few epithelial cells. On boiling, a dense cloud of albumen appeared.

In the blood, no parasites were found. A differential count of the white cells gave the following result:

This patient was treated with quinine, thirty grains of the bihydrochloride, by intramuscular injection, each day. Calcium chloride and adrenalin were also given. His urine became clear on the fourth day and he recovered.

Case 8. September 6th, 1913.

A Chinese goldsmith from Rembau in Negri Sembilan. This man had suffered from frequent attacks of fever for which he took quinine irregularly. Three days before his urine was examined here, he took ten grains of quinine and when he next passed water it was black. Two days later he was admitted to the Seremban Hospital. No parasites were found in his blood. The slides sent to this Institute were damaged in transit so that a reliable estimation of the numerical proportions of the white cells could not be made. The urine was almost black. It contained oxyhaemoglobin, and "haemoglobin" casts with a few adherent epithelial cells. On boiling, it was almost solid with albumen.

This patient was treated with quinine, twenty grains of the bihydrochloride by intra-muscular injection every day. The temperature became normal and the urine clear on the sixth day.

Case 9. September 19th, 1913.

A European, planter, aged about 30, from an estate (Jalan Acob) in Kuala Selangor. This patient had suffered from frequent attacks of malaria for several years. Two years before he had suffered from a previous attack of blackwater. During the four weeks immediately preceding his present illness he had been suffering from fever and had been taking ten or fifteen grains of quinine every day. The attack began with vomiting, diarrhoea and the passing of black urine.

No parasites were found in his blood. The result of a differential count was as follows:

The urine, examined on the third day of this patient's illness, was so dark that it appeared to be black, until it had been diluted. It contained oxyhaemoglobin, granular "haemoglobin" casts with adherent epithelial cells and a large amount of albumen. The patient was treated with quinine, fifteen grains of the bilydrochloride every day, and saline injections. On the fifth day there was still a cloud of albumen when the urine was boiled, and a trace of oxyhaemoglobin could be detected by spectroscopic examination; there were also a few small casts and some large epithelial cells in the urine. On the following day the urine was clear of haemoglobin, but there was still a trace of albumen and granular casts were still present on the eighth day. His illness ended in recovery.

Case 10. September 22nd, 1913.

A Chinese carpenter, aged 26, from Seremban town. This man had worked on a rubber estate in Singapore where he had suffered much from malaria. During the five months prior to his present attack he had been living in Seremban where he had been ill with malaria nearly the whole time and had taken quinine irregularly. He was admitted to the Seremban Hospital on September 20th, with a wound on his foot, and, during the night, he had an attack of fever. His blood was examined, subtertian rings were found and quinine was administered. He received an intra-muscular injection of ten grains of the bihydrochloride of quinine on the afternoon of September 21st, and a second injection the next morning. Three hours after the second dose, he passed black urine. The injections of quinine were not discontinued; another dose of ten grains was given four hours after the appearance of the blackwater and twenty grains were injected during the course of the following day (23rd September). The urine had cleared by the next morning, within twenty-four hours of the commencement of the attack. One more injection of quinine was given and thereafter thirty grains a day by the mouth.

No parasites were found in the blood-smears made on September 24th. White cells were present in the following proportions:

## Case 11. October 6th, 1913.

A Ceylonese clerk, aged 25, from Seremban. He had lived in the Malay States for five years. He is employed in the Federated Malay States Railways and, for some time before his attack of blackwater, he had been on duty as a relief-clerk, going from place to place to act for such members of the staff as were ill or were absent on short leave. In May, he contracted malaria at Perhentian Tinggi in Negri Sembilan and, since then, he had had about twenty attacks of fever for which he took quinine irregularly. He had never suffered from blackwater before.

On October 3rd, he was admitted to Seremban Hospital suffering from subtertian malaria. He was given thirty grains of quinine sulphate on each of the first two days after his admission. Three days later—that is on October 6th, he had a rigor, his temperature rose to  $103^{\circ}$  and he passed black urine. In the evening his temperature came down to normal and did not rise again. No parasites were found in his blood after the appearance of the blackwater. The administration of quinine was not suspended: twenty grains of the bihydrochloride of quinine were injected into the muscles, daily, for the next four days, and thereafter he received thirty grains a day by the mouth. Vomiting was severe and lasted for twelve days. The patient recovered.

The urine on the day of the attack of blackwater was so dark that it was necessary to dilute it four times before it could be examined with the spectroscope. On boiling, it became solid with coagulated albumen. There was a plentiful brown deposit which contained renal casts of amorphous blood-debris, but consisted, principally, of a loose deposit of the same material. Spectroscopic examination demonstrated the presence of oxyhaemoglobin.

## Case 12. October 14th, 1913.

A Tamil, aged 15, from Bongsar, near Kuala Lumpur. This boy had lived at Bongsar for a year. He had suffered a good deal from subtertian malaria and had an enlarged spleen. Before this attack of blackwater he had not had fever for a month; but, on the 12th of October, he became ill and the estate dresser gave him quinine: ten grains of the bihydrochloride in a mixture. On the 13th, the fever continued and he was given twenty grains of quinine in two doses. On the 14th, he still had fever and at 8 o'clock, ten grains of quinine were administered. Three hours later he passed dark, blood-coloured urine, his pulse became rapid and he was very ill.

The urine resembled pure blood and it was necessary to dilute it five times before it could be spectroscopied satisfactorily. On boiling it became a solid cake of coagulated albumen. The deposit, after centrifuging the urine, was small and consisted of amorphous blood-debris and a few small "haemoglobin" casts. The spectroscope showed the presence of oxyhaemoglobin and methaemoglobin.

The blood contained no parasites. There were a few normoblasts but no poikilocytosis.

The white cells were in the following proportions:

Polymorphonuclears	...	...	...	...	...	...	...	65.7
Lymphocytes	...	...	...	...	...	...	...	16.6
Large Mononuclears	...	...	...	...	...	...	...	17.4
Eosinophiles	...	...	...	...	...	...	...	.3

On the 15th, the patient's fever continued; but his urine, though still red, was of a far lighter tint than on the previous day and it was easy to see the oxyhaemoglobin bands without previous dilution. Schlesinger's test demonstrated the presence of urobilin with the characteristic band near the F. line of the spectrum. When boiled, the urine no longer became solid, but only a thick cloud of albumen was coagulated. As on the previous day, the deposit contained small haemoglobin casts, but, in addition, there were some large casts of the same material, probably from the collecting tubules, and also epithelial casts and large epithelial cells.

On the same day 2 c.c. of blood were withdrawn from the median basilic vein. This blood was divided into two equal parts: 1 c.c. was allowed to clot in a test-tube and 1 c.c. was poured into a solution of sodium citrate. Twenty-four hours later an examination was made of the serum in the one tube and of the supernatant fluid in the other; in both cases the fluid was of an intense yellow colour, there was no pink tinge. The spectroscopic examination of the serum showed the presence of a trace of methaemoglobin, but in the citrate solution none could be seen. When ammonium sulphide and caustic potash were added to the two tubes, there appeared well-marked bands of haemochromogen. The blood was more watery than on the previous day and in the smears the red cells showed some degree of poikilocytosis and a few normoblasts. The leucocytes were present in the following proportions:

Polymorphonuclears	...	...	...	...	...	...	...	68
Lymphocytes	...	...	...	...	...	...	...	19.6
Large Mononuclears	...	...	...	...	...	...	...	12.4

On the afternoon of the same day, 15th October, the temperature fell to normal and, the next morning, the urine became clear.

## Case 13. October 20th, 1913.

A European, planter, aged 27, from Branscombe Estate, Batu Tiga, in the State of Selangor. He had been in the country for four years. During the three months preceding his attack of blackwater he had suffered from fever twice a week and, on this account, he had been taking fifteen grains of quinine every day.

On October 20th, he passed a pint and a half of dark red urine. He was admitted to the European Hospital, Kuala Lumpur, on the evening of 21st October. No parasites were found in his blood. His temperature was 104°F. He was vomiting frequently and complained of severe pain in the pit of the stomach. His skin was saffron-coloured. His spleen was enlarged. From the time of admission to the hospital, until his death forty-five hours later, he passed only four and a half ounces of urine; during the last twenty-four hours there was complete suppression. The patient was given large quantities of saline solution per rectum and quinine by the mouth, but, as he vomited everything, he could have absorbed little or no quinine. He died on 23rd October, less than sixty-seven hours after the onset of his illness.

The urine was the colour of porter and contained a copious deposit which consisted, almost entirely, of haemoglobin in the form of minute irregular globules. Some of these formed tubular casts, many of them being of large size. The most striking feature of the deposit was the presence of a large number of epithelial cells, some of them round, some oval and some pyriform. Many of them contained two nuclei and all of them were stained brown. The spectroscope showed that the urine contained oxyhaemoglobin. It was necessary to dilute the urine five times before it could be spectroscopied. On boiling the urine became solid with albumen.

The blood was examined on the second day of illness and again on the day of the patient's death. On the latter day, half a cubic centimetre of blood was drawn from a vein in the arm and put into 10 c.c. of citrate solution. The supernatant fluid, after twenty-four hours, was bright yellow colour resembling a solution of picric acid. No haemoglobin bands were seen but on adding ammonium sulphide and caustic potash the absorption bands of haemochromogen were very clear. A differential count made on the 21st October gave the following result:

Polymorphonuclears	...	...	...	...	...	...	67 per cent.
Small Lymphocytes	...	...	...	...	...	...	17 "
Large Mononuclears	...	...	...	...	...	...	16 "

No malarial parasites or normoblasts were found on either day. On the second day the blood was so watery that it was difficult to make satisfactory blood-smears. In both specimens there were many broken polymorphonuclear leucocytes.

## Case 14. October 30th, 1913.

A Tamil, clerk, aged 33, from Cheviot Estate in Negri Sembilan. He had been in the Malay States for three and a half years, during the whole of which time he had been employed on the same estate. He took quinine whenever he had fever, but not at other times.

Three weeks after his arrival, he had an attack of fever, and, during the first year of his stay, he had fever about once a week. Throughout the second year, he had fever once a month and, during the third year, he suffered from occasional attacks which lasted a few hours but were never severe enough to prevent him from doing his work. He had never suffered from blackwater before. He had fever on the 28th September and took twenty grains of quinine. The next morning he passed black urine and vomited. He was admitted to the Seremban Hospital on the 30th September. His temperature was 101.4°F.; but it came down to normal in a few hours and did not rise again. His spleen was enlarged and reached a little below the umbilicus. He was treated with quinine: twenty grains of the bihydrochloride injected into the muscles daily. The urine cleared after forty-eight hours and he recovered.

The urine passed on the 30th September, the second day of his illness, was of a brownish-red colour. On boiling, a cloud of albumen appeared. The deposit in the urine was not very copious. It consisted almost entirely of minute globules of haemoglobin which measured one to two micromillimetres in diameter and stained, like erythrocytes, a bright red with eosin or fuchsin. There was a small number of casts in the deposit, composed of haemoglobin spherules and a very few cells. Spectroscopic examination showed the presence of oxyhaemoglobin.

The serum from a specimen of blood drawn on the third day of this patient's illness, after the urine had cleared, was rather highly coloured. No haemoglobin bands could be detected by the spectroscope. No parasites were found in the blood. The white cells were present in the following proportions:

Polymorphonuclears	...	...	...	...	...	...	55.5
Lymphocytes	...	...	...	...	...	...	27.5
Large Mononuclears	...	...	...	...	...	...	13.5
Eosinophiles	...	...	...	...	...	...	3.0
Mast cells	...	...	...	...	...	...	0.5

## Case 15. November 14th, 1913.

A European, planter, aged 28, from Colwall Estate, Kajang, in the State of Selangor. He had been three years in the Federated Malay States and had always worked on the same estate. A few years ago, this estate was notoriously unhealthy, but, now, it has greatly improved, though the spleen-rate is still high. This patient had suffered from tertian malaria about four months before he was attacked with blackwater, but, apart from that, he had been unusually free from fever for some time. He did not take quinine except when he was suffering from fever.

On November 14th he had fever and took twenty-five grains of quinine sulphate, in two doses; five hours after the second dose he had a rigor and passed black urine. On the following day he was admitted to the European Hospital at Kuala Lumpur. The urine remained dark until the fourth day when it was a little lighter in colour. It cleared on the fifth day, when no haemoglobin could be detected by spectroscopic examination. Throughout his illness, this patient passed large quantities of urine. During the first day he passed about fifty ounces and thereafter over one hundred ounces in each twenty-four hours.

The urine was dark-red in colour and spectroscopic examination showed that it contained oxyhaemoglobin and a little methaemoglobin. On boiling, it became solid. The deposit contained blood-debris and haemoglobin casts.

The patient's temperature remained high throughout the course of his illness. He had several rigors and vomited frequently. Though the urine cleared on the fifth day the patient did not recover but died early on the seventh day.

No parasites were found in the blood of this patient after the onset of the blackwater. On the second day of his illness the white cells were present in the following proportions:

Polymorphonuclears	...	...	...	...	...	...	...	37
Lymphocytes	...	...	...	...	...	...	...	40
Large Mononuclears	...	...	...	...	...	...	...	22.5
Mast cells...	...	...	...	...	...	...	...	0.5

Two days later the numbers were:

Polymorphonuclears	...	...	...	...	...	...	...	51.3
Lymphocytes	...	...	...	...	...	...	...	30.0
Large Mononuclears	...	...	...	...	...	...	...	17.6
Eosinophiles	...	...	...	...	...	...	...	.5
Mast cells...	...	...	...	...	...	...	...	.6

Seventeen hours after the commencement of the attack a specimen of blood was withdrawn from the patient's arm and allowed to clot. The resulting serum was red and matched a 0.25 per cent. solution of normal blood in distilled water. It contained oxyhaemoglobin. In a second specimen drawn two days later, when the urine was beginning to clear, the serum was no longer red but orange-coloured. No haemoglobin could be detected in it by spectroscopic examination.

*Post-mortem.*—Examined eight hours after death, all the tissues were found to be stained yellow. There appeared to be but little blood in the body and it was pale and watery. The spleen was slightly enlarged and, though rigor mortis was present in the limbs, it was diffused. A few old adhesions passed from it to the abdominal wall.

**Liver.**—In the outer, portal zones of the lobules there was but little alteration from the normal condition. The liver cells were slightly swollen and some of the nuclei did not stain well. In this zone there were fine granules of a dark sepia-coloured pigment along the centre of the trabeculae. This pigment contained iron in loose organic combination, readily set free by dilute mineral acids. Towards the inner part of the portal zones the trabeculae were broken up and the cells contained a light yellow pigment mixed with the dark granules already mentioned. At the centre of each lobule the liver tissue had undergone profound destruction. The parenchymatous cells were broken up into rounded masses containing yellow pigment which did not contain free iron or iron in loose organic combination. In this central zone the number of nuclei was increased; prominent among them were some which stained darkly and were multilobed or undergoing division. This increase of nuclei was in no sense the result of a small-cell infiltration, it was more apparent than real, being in part, at any rate, an aggregation of the nuclei of the connective tissue, the strands of which had come together owing to the absorption of the intervening parenchymatous cells. In some of the lobules haemorrhage had occurred into the central zone of disintegration. There was no fatty infiltration or fatty degeneration. The vessels and ducts in the portal capsules appeared to be normal.

**The Spleen.**—This organ contained a rather large amount of malarial pigment. No malarial parasites were seen. The increase in size was due to an hyperplasia of the pulp. A striking feature, in the sections of this organ, was the comparatively small number of the red blood corpuscles.

**The Kidney.**—There were but slight pathological changes in this organ. The glomeruli were normal. In the lumina of the convoluted tubules there was an amorphous, granular deposit which contained iron in organic combination. There was also a little iron in the

epithelial cells lining these tubules. There was no blocking of Henle's tubes, or of the collecting tubes, with masses of blood-debris. The capsule of the kidney and the connective tissue were normal. The capillary vessels of the cortex were slightly dilated and contained a quantity of pigment in the form of intensely black granules, which did not give the reactions of iron. Much of this pigment had been taken up by the endothelial cells of the vessels so that they were outlined with black.

**Case 16. November 27th, 1913.**

A European, planter, aged 24, from Dindang Estate, Siputeh, in the State of Perak. He had worked on this estate for two and a half years but left it a month before his illness and, during that month, he had been living in Ipoh. He had fever very frequently and had taken quinine irregularly. He had never had blackwater before.

On 25th November he had fever with rigors and took two grains of quinine sulphate. During the night he vomited and at 8 a.m. on 26th September he passed dark urine. He was admitted to Batu Gajah Hospital on the same day, five hours later, with a temperature of 101.6° F. He had a rigor a few hours afterwards. There was a little vomiting on the 27th. His spleen was palpable and he was rather yellow. During the first twenty hours after his admission he passed thirty-two ounces of urine. He was treated with perchloride of mercury and also received small doses of quinine for the first few days. The urine became clear of blood in about twenty-four hours and the patient soon recovered.

*Urine.*—The urine passed in the early part of the first day of his illness was of a red colour. Spectroscopic examination showed that it contained methaemoglobin. There was a deposit, not very copious, which was composed of haemoglobin debris in globular form, casts of the same material, a few epithelial cells and some ammonium biurate. Albumen was present in considerable quantity.

The urine passed during the afternoon and night of 26th November (the first day) was considerably lighter in colour and could be examined easily by the spectroscope without diluting it. Methaemoglobin was still present in small amount. The deposit was of the same character as in the earlier specimens but it contained more ammonium biurate. The urine passed during the next morning, 27th November, was apparently clear of blood. A specimen passed at 10.30 a.m. was of a bright yellow colour. The spectroscope did not show the presence of blood. Ammonium biurate crystals were present, and a few granular haemoglobin casts with a number of adherent epithelial cells.

*Blood.*—In this case the white blood cells were present in the following proportions:

Number of hours after commencement of attack.	6	12	26	30
Polymorphonuclears	68.4	68.7	64	60
Lymphocytes	14	14.7	19.5	23.5
Large Mononuclears	15.2	15.3	10.5	12
Eosinophiles	2.4	1.3	6	4.5

On the day of this patient's admission to hospital, about six hours after the commencement of the attack and when he was passing black urine, a few crescents and young simple tertian parasites were found in his blood. On the evening of the same day malarial parasites were still present and they were found again on the following day, after the urine had become clear of blood. Malarial pigment was seen in some of the polymorphonuclear cells. Basophile grannules were observed in many of the corpuscles but there was no poikilocytosis, nor were any normoblasts present.

On the second day of this patient's illness, 27th November, a sample of blood was drawn off from the median basilic vein. At this time the urine was free from haemoglobin but contained a little albumen. The serum was of a yellow colour, much darker than usual, but the spectroscope did not show the presence of haemoglobin.

This serum agglutinated a certain sample of normal corpuscles very strongly and the corpuscles of this case were agglutinated, but not so strongly, by the serum of this same normal case.

**Case 17. November 27th, 1913.**

A Japanese, female, aged 33, from Senawang Estate in Negri Sembilan. She had lived for twelve years in the Federated Malay States. Occasionally she suffered from slight fever, and, as a rule, took a capsule of quinine sulphate every three or four days. On 25th November she had fever and took five grains of quinine. On 26th she was better and again took five grains of quinine. On 27th November at 6 a.m. she passed black urine. On the same day she again took five grains of quinine. On the following day, 28th November, she was brought to the Seremban Hospital. She was retching and vomiting. Her temperature was 100° F. She was passing very little urine. It was not measured. She was given thirty grains of quinine bihydrochloride, intra-muscularly, in three doses, between the time of her admission and her death which took place twenty-four hours later.

*Urine.*—A sample of urine passed on 28th November, when she was admitted to Seremban Hospital, was dark-red in colour and it was necessary to dilute it four times before it could be examined satisfactorily with the spectroscope. It contained oxyhaemoglobin but no methaemoglobin. On boiling, the urine became almost solid with coagulated albumen. The deposit contained much amorphous blood-debris and many casts of the same material. Some of the casts contained a few epithelial cells and some were entirely cellular.

*Blood.*—The blood slides prepared from this case were unfortunately spoiled by damp in transit, so that no blood count could be made. No malarial parasites were found.

#### Case 18. November 26th, 1913.

A Malayalum, aged 40, a cooly on Sungai Tinggi Estate, Kuala Selangor, in the State of Selangor. He had been four months in the country. Two months before his attack of blackwater he had suffered from fever. During the last two months he had not taken more than three or four doses of quinine and he had received none for more than a week before the onset of the blackwater.

On 25th November he was admitted to Rantan Panjang Hospital suffering from fever. Dr. Harrison examined his blood and found that malarial parasites (subtertian rings) were present. No quinine was given that day, and, on the following morning, 26th November, he passed black urine. He was treated with quinine bishydrochloride. The urine cleared in forty-eight hours and he recovered.

*Urine.*—The urine passed on the first day of the attack contained oxyhaemoglobin. There was a deposit which consisted of amorphous blood-debris and a few casts. On boiling, a cloud of albumen appeared. On the third day, 28th November, no haemoglobin could be detected by spectroscopic examination, and there was no albumen present. Schlesinger's test demonstrated the presence of a quantity of urobilin so considerable that it was necessary to dilute the urine before the characteristic band, near the F. line, could be seen with the spectroscope.

*Blood.*—Though malarial parasites were present on the day before the attack of blackwater, none were found after it had begun. The most striking feature of the blood-smear was the large number of nucleated red cells which formed no less than 13.7 per cent. of the corpuscles.

The white cells were present in the following proportions:

Polymorphonuclears	...	...	...	...	...	...	...	50
Lymphocytes	...	...	...	...	...	...	...	31.7
Large Mononuclears	...	...	...	...	...	...	...	17
Eosinophiles	...	...	...	...	...	...	...	.7
Mast cells	...	...	...	...	...	...	...	.6

#### DYSENTERY.

The researches on this subject were in the first instance concerned with the amoebic form of the disease.

It is now generally agreed that the life-cycle of *Entamoeba histolytica* as described by Schaudinn was inaccurate and that the one described by Viereck for his new species *E. tetragena* is the correct one for *E. histolytica*. Since for what is now considered to be but one species the two investigators have each furnished a part of the correct description it has been urged that a new species—namely, *E. dysenteriae*, should be created and that the names *E. histolytica* and *E. tetragena* should be dropped. Such an arrangement would only tend to increase the confusion and for practical purposes it will probably be found most suitable to retain the specific name *Entamoeba histolytica* which has been well established by custom and usage. There can be no doubt but that of recent years there has been too great a tendency on the part of some investigators to group, frequently on quite insufficient grounds, the pathogenic amoebae into various species which more careful investigations have shown are but varieties of one pathogenic species. The clinician will find it best to treat the cases of dysentery in which amoebae are found in the stools as amoebic forms of that disease without attempting to append specific scientific names to the protozoa found.

Our attempts to cultivate the pathogenic amoebae have been uniformly unsuccessful; results which are in accordance with those of all recent workers.

As regards the bacillary form of this disease the exciting organism has so far only been isolated from a limited number of acute cases and has in each instance corresponded with the Bacillus Y. of Hiss and Russell. Further investigations will perhaps furnish us with the other types of dysentery bacilli and it is hoped to prepare a serum or sera for use in cases of bacillary dysentery.

#### ACUTE DYSENTERY WITH LARGE NUMBERS OF SPIROCHÄTES IN THE FÆCES.

In this case a male Tamil child, six years of age, was taken ill suddenly with vomiting, diarrhoea and abdominal pains. The temperature rose to 104°F. No malarial parasites were present in the blood. The fever subsided and the vomiting ceased in two or three

days, but the diarrhoea continued, and, at intervals of thirty minutes, or less, the child passed green slimy stools which were sometimes mixed with blood. When this case was first brought to our notice, on the ninth day of the disease, the child appeared to be moribund; but, from that time, the distressing symptoms began to abate and, eventually, the child recovered. Two little girls, sisters of this child, and living in the same house, were taken ill with similar symptoms and one of them died. The faeces of the first child were brought to the Institute, and were examined, on the eleventh day of the disease. Spirochaetes were present in enormous numbers; far exceeding all the other organisms present. Examined by the dark-ground microscope, the faeces were alive with spirochaetes; some free, some gathered into skeins and radiating tangled masses. The majority of the organisms were short, measuring on an average 5.25 microns and with only one or two curves. The extremities were tapering. The width of the curves varied in different specimens; for instance, one spirochete, with four curves, measured 9.6 microns, while another, lying close to it, but having only two curves, measured 8.8 microns. The organisms were of the *refringens* type, with wide and irregular curves which changed their position and shape with the movements of the spirochete. These movements, which were very energetic, were of a snake-like, lashing character.

Broth and agar media inoculated with the faeces, and also a tube of the faeces themselves, were kept over-night at a temperature of 37° C. On the following morning no spirochaetes could be found in the agar tubes or in the faeces. In the broth there were a very few dying, or inactive, spirochaetes. In a second sample of faeces passed at 9 a.m. on the morning after the first examination was made, very few spirochaetes were present and, in subsequent stools, passed a few hours later, none could be found. It was impossible to obtain samples of faeces from the other two children, who were taken ill in the same house, except on one occasion, and then no spirochaetes were found.

#### THE WASSERMANN REACTION.

Seventy-three patients were examined by Wassermann's reaction for syphilis. In forty-nine instances in which the disease was latent, or where the examination was undertaken in order to clear up a doubtful diagnosis, the result was positive in ten, and negative in thirty-nine cases. Seven persons in the secondary stage of the disease, and seventeen with active tertiary lesions, were also examined, the result being positive in every case.

The method employed for this test was that of Browning, Cruickshank and Mackenzie, the distinguishing feature of which, is the use of two antigenic extracts: one of ox-liver lecithin and another consisting of a mixture of lecithin and cholesterol. The authors of this modification found that, in the ordinary methods of carrying out the test, a normal serum, in the presence of an emulsion of organ extract, may absorb more complement than the sum of the amounts absorbed by the serum and the emulsion separately; so that, in such cases, the reaction is apparently positive. They overcame this difficulty by the employment of the two antigens mentioned above and they found that "if a serum absorbs more complement in the presence of lecithin plus cholesterol than it absorbs in the presence of lecithin alone, then this is evidence of its syphilitic nature."

Browning, Cruickshank and Mackenzie employed an anti-oxhaemolytic system. The use of this system entails the previous saturation of the guinea-pig serum with ox-corpuscles and centrifugalisation at 0° C. in order to remove the natural amboceptor which may be present. In order to obviate this difficulty the haemolytic system employed here was that in which human corpuscles are sensitised with the homologous immune serum from the rabbit.

#### THE LUETIN REACTION.

Dr. Fletcher furnishes the following report:

Luetin consists of killed cultures of the *Treponema pallidum* emulsified with the media in which they have grown. It has been shown to produce a localized inflammatory reaction when injected into the skin of syphilitics.

These investigations were carried out with a sample of luetin kindly supplied by Dr. Noguchi of the Rockefeller Institute.

#### THE PREPARATION OF LUETIN.

Soon after Noguchi had succeeded in obtaining pure cultures of the *Treponema pallidum* he commenced to study the effects of the inoculation of killed cultures as an aid to the diagnosis of syphilis. For this purpose he used an emulsion prepared in the following manner.

An agar culture of the *Treponema pallidum* was ground up in a mortar. The resulting thick paste was gradually diluted by the addition of a culture of the same organism in ascitic fluid, until the emulsion became perfectly liquid. The preparation was then heated at 60° C. for one hour and 0.5 per cent. carbolic acid was added. This preparation he named *Luetin*. As a control he used a carbolized emulsion prepared from similar media which had not been inoculated with the *Treponema pallidum*.

## NOGUCHI'S EXPERIMENTS.

Noguchi's first experiments were made with rabbits. He found that rabbits which had received twelve intravenous inoculations of living or killed cultures of the *Treponema pallidum*, during a period of five months, gave an allergic reaction when (after an interval of two months from the last injection) a *déchainante* dose of luetin was injected into the skin. Normal rabbits, rabbits suffering from experimental syphilitic orchitis and rabbits which had been cured of orchitis by salvarsan, all reacted negatively to injections of luetin.

Noguchi next tested his preparation on man. He found that in the majority of normal persons, twenty-four hours after the injection, a small erythematous area appeared at the point of inoculation, which subsided in forty-eight hours. On the other hand, in the skin of syphilitic persons, the injection of luetin frequently produced certain well-defined lesions of which he distinguished the following three forms:

(1) *The Papular Form.*—An indurated papule, five to ten millimetres in diameter, appears in twenty-four to forty-eight hours. The papule increases until the fourth or fifth day after which it subsides gradually and disappears by the end of the second week.

(2) *The Pustular Form.*—The reaction pursues the same course as the papular form until the fifth day when, instead of becoming smaller, it increases in size, the central portion softens and a vesicle forms which rapidly becomes pustular. This ruptures, and a scab forms which falls off in a few days. There is a wide range in the intensity of this reaction. Noguchi found that this form occurred almost constantly in tertiary syphilis and also in cases of secondary and hereditary syphilis which had been treated with salvarsan.

(3) *The Torpid Form.*—In rare instances, though no positive result follows the injection during the first ten days, at the end of that time, or after an even longer interval, a pustular reaction occurs.

Noguchi found that, in syphilitics, the reaction to luetin varied according to the stage of the disease and the kind of treatment the patient had received. In untreated primary and secondary cases the result was generally negative, occasionally there was a papular reaction. In secondary cases treated with salvarsan the result was positive in more than seventy per cent. In tertiary and hereditary cases the reaction was intense and almost constantly positive. Noguchi's reported cases comprised 177 syphilitics and 146 controls; none of the controls reacted positively. As the result of his investigations he concluded that, whereas the Wassermann reaction is more consistently positive in primary and secondary syphilis, the luetin reaction is more constant in the tertiary and latent forms; moreover, the luetin reaction is less directly and immediately affected by antisyphilitic treatment than the Wassermann reaction. He considers that the cutaneous reaction should prove to be of great value in the diagnosis of syphilitic lesions of the internal organs.

## EXAMINATION OF THE SPECIMEN OF LUETIN EMPLOYED IN THIS INVESTIGATION.

This specimen had been prepared at the Rockefeller Institute from six strains of *T. pallidum* killed by exposure to a temperature of 60° C. for one hour and preserved by the addition of 0.25 per cent. trikresol.

There was unfortunately some delay in the post, and, during that time, the specimen of luetin must have been exposed to comparatively high temperatures. After the phial containing it had been received it was stored in a domestic ice-chest at a temperature of 20° C. Dr. Noguchi recommends that it should be kept in a refrigerator. There was a further delay before it was possible to employ it. The phial was despatched from the Rockefeller Institute in January, 1913, but the first cases were not inoculated until the following September.

Noguchi states that luetin, when examined under the dark-field microscope, is seen to contain about seventy dead *pallida* in each field. The specimen of luetin, used here, was examined soon after it was received, when less than a tenth of this number could be recognized; they were mixed with small masses of debris and broken spirochaetes. Re-examination, about three months later, showed that the number of free and unaltered organisms was still less, only one or two in each field; the number and size of the masses of debris had increased and it appeared that they consisted, largely, of agglomerations of spirochaetes. These observations show that the storage had some effect upon this preparation of luetin and it may be that, from this cause, its efficiency became impaired.

On many occasions tubes of agar were inoculated with the luetin in order to ascertain if it had become contaminated by bacteria or moulds. The tubes always remained sterile.

## THE CONTROL EMULSION.

A control emulsion was prepared according Noguchi's original method. Two per cent. agar was ground up in a mortar and ascitic fluid was added until a mixture was obtained which passed readily through a fine hypodermic needle. Carbolic acid was added to the amount of 0.5 per cent. The fluid was put up in glass capsules, each containing 0.5 c.c., and these were heated for one hour at 60° C.

## METHOD OF INOCULATION.

The skin of both forearms was rubbed with pledges of cotton-wool, soaked in a solution of Kymol. The injections were made, not subcutaneously, but into the superficial layers of the skin. In each instance, the luetin was injected into the left forearm and the control emulsion into the right. The amount recommended by Noguchi for each inoculation is 0·07 c.c., consisting of equal parts of luetin and physiological saline solution. A syringe capable of measuring this dose was not available; so that a ten-minim syringe was employed and one minim of equal parts of luetin and 0·9 per cent. salt-solution was injected into the left forearm of each case and one minim of the control emulsion into the right.

## TYPES OF REACTIONS OBTAINED.

The total number of persons inoculated was 108. In twenty-two cases there was a positive reaction.

(1) *Papular Form*.—Among the twenty-two positive cases there were only four simple papular reactions (Nos. 1 to 4). These comprised two cases of primary syphilis and two of tertiary. In these cases a small, red, itching papule persisted at the site of the luetin inoculation after all signs of the control inoculation had disappeared. On the sixth day, in each instance, the papule was about the size of a pea; a few days later it had become absorbed.

(2) *Pustular Form*.—There were twelve pustular reactions; one in primary, three in secondary and eight in tertiary cases (Nos. 4 to 15). In these cases the papule persisted at the site of the luetin inoculation. It became inflamed and its size increased. On about the sixth day it became darker and cyanosed. Fluctuation developed in the centre, the margin remaining indurated. The lesions were rather abscesses than pustules; in some instances they measured as much as 4 cm. in diameter. There was very little tenderness or pain associated with them, the principal subjective symptom was itching. In one case (No. 13), there was some general disturbance; the patient's temperature rose to 100°-101° F., and he had pains in the back and limbs for twenty-four hours. So greatly did these abscesses resemble septic lesions that, in several of the earlier cases, the contents were drawn off with an aspirating syringe and inoculated on agar tubes, but these always remained sterile. When the curdy pus from these lesions was examined under the microscope, it was seen to consist of tissue-debris, mononuclear cells, polymorphonuclear cells and erythrocytes. No spirochaetes were ever seen.

In eight of the twelve pustular cases the reaction reached its maximum on the fifth to the eighth day. In three it continued to increase until the eleventh or twelfth day after inoculation.

In some of the pustular cases the abscess burst and discharged its contents, after which it subsided rapidly; in other cases the contents were absorbed without rupture taking place. In the latter event, the softened central part was absorbed earlier than the indurated margin; the result was a swelling with hard edges and a crater-like softened centre. After the lesion had disappeared a discoloured patch marked the place where it had been; the depth of pigmentation depending largely on the amount of pigment in the patient's skin. This pustular form of reaction had generally run its course in from two to four weeks. In addition to the three types of reaction described by Noguchi, a fourth variety has been observed, a recurrent pustular form. In two of the cases (No. 7 and No. 9) the reaction was of a recurrent nature; that is to say, when it had run its usual course and after an interval of a week or more, a secondary inflammation occurred in the same spot. In both cases this secondary inflammation reached its maximum more quickly than the primary lesion and subsided in a shorter time. In case No. 7, the abscess attained its greatest size on the eighth day, after which it subsided gradually; but, at the end of the third week, it again increased in size, so that by the end of the fourth week it was nearly as large as it had been at the end of the first. In Case No. 9 the reaction recurred after an interval of more than four weeks.

(3) *Torpid Form*.—Noguchi found that this form occurred but rarely. With the specimen of luetin employed here, possibly on account of the changes which it had undergone during transit and storage, the proportion of torpid reactions was comparatively large. Five instances occurred in cases of latent tertiary syphilis and two in cases of tabes (Nos. 16-22). In the ordinary papular and pustular reactions, the papule at the site of the luetin injection does not disappear, but gradually increases until it attains its maximum development; on the other hand, in these seven torpid cases, the minute papules produced in the skin by the presence of the fluid of the control and luetin injections disappeared entirely; but, after an interval of from eight to twenty days, a red papule appeared at the point of injection of the latter. In three cases these papules did not suppurate: in four, suppuration occurred and the reaction resembled the ordinary pustular form except for its latency.

## REACTION AT THE SITE OF CONTROL INOCULATION.

In three cases, one of primary, one of secondary and one of tertiary syphilis (Nos. 5, 7 and 10) there was a reaction at the site of the control inoculation; in case No. 7 this was so severe that a small, sterile abscess formed. But the luetin reaction in this case was much more marked than the control; the abscess was larger and of considerably longer duration. In the other two cases the control reaction was less severe than in case No. 7 and did not

progress beyond the papular stage, while at the site of the luetin inoculation, in both cases, the reaction was pustular and prolonged. In 177 cases of syphilis, Noguchi observed nine in which there was a definite reaction at the point of inoculation of the control emulsion, but it was never so severe as the reaction produced by the luetin injection in the same case. He points out that the skin of syphilitics is noted for its susceptibility to traumatic irritation and that Finger has advanced the theory that the syphilitic virus, within the body, attacks the spot where resistance has been lowered by the injury, while, on the other hand, Neisser maintains that this increased irritability is due to a pathological condition of the skin itself.

#### PARTICULARS CONCERNING PATIENTS INOCULATED.

The number of persons inoculated with luetin was 108. They were divided into four groups:

- (1) Thirty-two patients suffering from syphilis;
- (2) Six doubtful cases;
- (3) Twenty-eight persons suffering from diseases other than syphilis.
- (4) Forty-two inmates of an infirmary, many of whom were likely to be syphilitic.

(1) *Syphilites*.—This group consisted of seven cases of primary, eight cases of secondary and seventeen cases of tertiary syphilis. Most of the patients had been treated with mercury, administered by the mouth or as an inunction. Only one had been given an injection of salvarsan.

As can be seen by reference to Table I, a positive reaction was obtained in fourteen out of the thirty-two cases.

Only eight of the thirteen cases of tertiary syphilis reacted positively, whereas Noguchi obtained nearly a hundred per cent. of positive reactions in this stage of the disease. The discrepancy in these results is probably to be explained by the age of the preparation of luetin used here.

In the cases of this group which reacted with luetin, the Wassermann reaction was positive in nine, negative in two and not examined in three. In the cases which did not react with luetin the Wassermann reaction was positive in fifteen, negative in two and not examined in one.

TABLE I (PATIENTS IN GROUP 1).

	Type of luetin reaction.			Total positive.	Total negative.	Total cases.
	Papular.	Pustular.	Torpid.			
Primary syphilis ...	...	2	1	3	4	7
Secondary (active) ...	...	...	2	2	3	5
Do. (latent) ...	...	...	1	1	2	3
Tertiary (active) ...	...	2	4	6	5	11
Do. (latent) ...	...	...	1	1	4	6
Total ...	...	4	9	14	18	32

(2) *Doubtful cases*.—None of the six cases in this group reacted with the luetin injection nor was the Wassermann reaction positive in any of them.

(3) *Patients suffering from non-syphilitic diseases*.—This group, consisting of twenty-eight persons, comprised the following:

Nine cases of beri-beri; twelve young lepers, all of whom were under nineteen years of age; six cases of malaria (quartan, simple tertian and subtertian); one case of yaws, with numerous and extensive lesions.

In none of the patients in this group was the inoculation of luetin followed by a positive reaction.

TABLE II (PATIENTS IN GROUPS 2 AND 3).

Disease.	Number of cases.	Reaction to luetin.
Doubtfully syphilitic ...	...	...
Beri-beri ...	...	...
Leprosy ...	...	...
Malaria ...	...	...
Yaws ...	...	...
Total ...	34	

Negative in all cases

(4) *Infirmary patients.*—This group consisted of forty-two inmates of the Tai Wah Hospital, which is an infirmary or home for Chinese, who, by reason of some incurable disability, the result of accident or disease, are unable to earn sufficient money to support themselves. More than half of the inmates of this Institution are blind; among this moiety are many cases of double optic neuritis, frequently of specific origin; but the commonest cause of their blindness is, probably, gonorrhœal ophthalmia.

In addition to these blind people and those crippled by accidents in mines and elsewhere, there are others who have been disabled from the results of syphilitic bone disease, myelitis and hemiplegia. In short, it appeared that, among these people, there might be many cases of latent tertiary syphilis of long standing and in such cases Noguchi has obtained a positive reaction in ninety-four per cent.

Of the forty-two patients in this group, eight reacted positively to the injection of luetin (Nos. 14, 15, 17, 18, 19, 20, 21 and 22). In two cases the reaction was pustular and in six it was of the torpid form. The proportion of torpid cases is very large. The Wassermann reaction in the eight cases which reacted to luetin was positive in four, negative in three and not examined in one. Table II shows the diseases from which the members of this group of patients were suffering and the cases which gave a positive luetin reaction.

TABLE III (PATIENTS IN GROUP 4).

		Negative luetin reaction.	Positive luetin reaction.	Total.
Disabled owing to injuries received in accidents	...	6	0	6
Hemiplegia	...	5	0	5
Spinal sclerosis following myelitis	...	2	0	2
Cataract	...	4	0	4
Senility	...	1	0	1
Ankylosis of hip joints	...	1	0	1
Amputation of leg owing to syphilitic necrosis	...	2	2	4
Double optic atrophy	...	5	2	7
Blindness following acute inflammation of eyes	...	8	4	12
Total	...	34	8	42

#### THE SPECIFIC NATURE OF THE REACTION.

Positive reactions with luetin were obtained in syphilitics only. None of the control cases reacted positively. On the other hand there were many cases of syphilis in which no reaction was obtained. Even in tertiary syphilis (where Noguchi obtained a positive reaction in almost every case) the results were most contradictory. To illustrate this point, two cases among the infirmary patients may be mentioned where the clinical condition was very similar, but where one gave a positive and the other a negative luetin reaction. Chay Yeong (No. 15) was thirty-nine years old, Chin Yoon was thirty-five; each bore numerous scars of tertiary syphilis; each had lost a leg, amputated for syphilitic necrosis; the serum of each of them gave a weakly positive Wassermann reaction, deviating five units of complement; they each received an inoculation of luetin upon the same day; but, while Chay Yeong reacted positively, Chin Yoon gave a negative reaction.

#### CONCLUSIONS.

The luetin examined here was at least nine months old; it would be wrong, therefore, from the results obtained with this single specimen, to draw any conclusions as to the general usefulness of this preparation in the diagnosis of syphilitic affections.

In no case did the luetin injection cause a reaction in non-syphilitic cases. Positive reactions occurred in syphilis only. So far it was specific; but a negative luetin reaction was of no assistance in determining whether a disease was or was not of a syphilitic nature. Even in tertiary syphilis, where Noguchi's results were almost constantly positive, nearly fifty per cent. of the cases gave a negative reaction.

In but one instance was the patient's general health affected and then only slightly and for a period of one day.

The local reaction was not painful; but as a rule the lesions produced were large and prominent and they frequently persisted for a long time, two to four weeks or even longer.

#### DETAILS OF POSITIVE CASES.

##### A.—PAPULAR FORM.

(1) *Wadiyer.*—A male suffering from primary syphilis. He had received no treatment. In this case a small papule developed at the site of the luetin injection. It reached its maximum size on the sixth day. It was never much larger than a pea and did not suppurate.

(2) *Anthermulugee*.—A male suffering from primary syphilis. He had received no treatment. A small, hard, red, itching papule developed at the site of the luetin injection which measured 0.5 cm. on the sixth day.

(3) *Chiang Ling*.—A male with active tertiary syphilis. He had received slight mercurial treatment. His serum gave a negative Wassermann reaction. On the third day after the inoculation of luetin there was a red papule which subsequently increased a little in size but did not suppurate. After the eighth day it disappeared slowly.

(4) *Ah Chan*.—A female with active tertiary syphilis. Her serum gave a faintly positive Wassermann reaction. In this case the luetin reaction was not very conspicuous. There was a small papule on the third day which gradually disappeared after reaching its maximum size on the sixth day.

#### B.—PUSTULAR FORM.

(5) *Raman*.—A male with primary syphilis. His serum gave a positive Wassermann reaction, deviating ten units of complement. He had received very little mercurial treatment.

After inoculation a red papule formed which suppurated and increased in size until the eleventh day when it formed a tense, painful abscess 4 cm. in diameter. Two days later, the abscess was less tense and painful and the centre was softening. It became absorbed slowly, leaving a black stain (the patient was a Tamil). In this case there was a slight, but definite, reaction at the site of the control inoculation, where a small papule formed which measured nearly 1 cm. in diameter on the eleventh day. It had almost disappeared three days later.

(6) *Ah Kew*.—A female with active secondary syphilis. Her serum gave a positive Wassermann reaction, deviating more than seven doses of complement. She had received a few inunctions of mercury. She reacted very intensely to the luetin inoculation. On the twelfth day the abscess measured 1.5 cm. x 3.5 cm. The central, fluid portion, was gradually absorbed, leaving an indurated margin which disappeared slowly.

(7) *O Yo See*.—A female with active secondary syphilis who had received moderate mercurial treatment. Her serum gave a positive Wassermann reaction, deviating five doses of complement.

She reacted very intensely to luetin. On the day following its administration there was a tender, red papule at the point of inoculation. This increased in size and softened in the centre until, on the eighth day, it had become an abscess measuring 2.5 cm. in diameter. From that time it gradually became smaller and had almost disappeared when, at the end of the third week, it again increased in size. On the thirty-third day it was fluctuating and almost as large as it had been on the eighth day. It did not rupture, but subsequently became absorbed leaving a brown stain.

In this case the control inoculation also produced quite an energetic response; on the fifth day there was an inflamed hard papule which soon softened in the centre and formed a small abscess nearly 1 cm. in diameter. The contents of this little abscess were drawn off with a syringe and proved to be sterile. Though the reaction at the site of the control inoculation was as great as some undoubtedly positive luetin reactions, it was much less intense and of much shorter duration than the reaction to leutin in this particular case.

(8) *Chooi Ying*.—A female with latent secondary syphilis, who had been treated with inunctions of mercury. Her serum gave a negative Wassermann reaction.

On the third day after the inoculation of luetin there was a surrounding areola of inflammation. By the fifth day, the papule had become more inflamed and measured 3 cm. in diameter. The central portion underwent softening and thus a small abscess was formed. This did not rupture but became absorbed in about a week.

(9) *Thaiammal*.—A female with active tertiary syphilis. She had been treated with mercury for a few days. Her serum gave a positive Wassermann reaction, deviating more than seven units of complement.

Following the injection of luetin, a large papule formed which measured 2.5 cm. in diameter on the fifth day. From that time it became smaller, softened in the centre and underwent absorption leaving a dark pigmented patch. Shortly afterwards this patient left the hospital. Nearly two months after she had received the injection of luetin, she was re-admitted suffering from a gumma of the thigh and it was noted that there was a recurrence of inflammatory activity at the site of the luetin injection in the left arm where there was a papule 3 cm. in diameter.

(10) *O Chin O*.—A female with active tertiary syphilis. She had received an injection of salvarsan five days before. Her serum gave a positive Wassermann reaction, deviating more than fifteen doses of complement.

After the control and luetin injections, red papules developed at the sites of both. The former persisted until the seventh day, by which time the luetin papule had increased in size and was softened in the centre. On the seventeenth day the latter measured a little more than 2 cm. in diameter and was fluctuating all over. The usual induration did not occur in the periphery of this abscess. Towards the end of the third week absorption commenced and was complete about a week later.

(11) *Loo Ping*.—A female with active tertiary syphilis. She had been treated with inunctions of mercury. Her serum gave a faintly positive Wasserman reaction, deviating four units of complement.

In this case there was an intense inflammatory reaction on third day, which reached its maximum on the seventh day when there was a furuncle, soft in the centre, with a hard margin. This subsequently ruptured and discharged its contents after which the surrounding induration disappeared.

(12) *Ah Yeow*.—A female with active tertiary syphilis. She had been treated for four weeks with inunctions of oleate of mercury which, owing to salivation, had been stopped for a week before she received an inoculation of luetin. Her serum gave a positive Wassermann reaction, deviating more than ten units of complement.

On the third day after the inoculation, there was a definite papule which increased in size so that on the fifth day it measured 2.5 cm. in diameter and was much inflamed. On the eleventh day it was larger and formed a swelling hard at the periphery, fluctuating in the centre and covered with red, congested skin. On the twelfth day the abscess was aspirated. The contents consisted of flocculent, pink, shreddy debris containing necrotic mononuclear and polymorphonuclear cells mixed with a smaller number of erythrocytes. Agar tubes, inoculated with this material, remained sterile. After the aspiration of this fluid, the abscess subsided leaving a dusky-red, desquamating patch which was 4 cm. in diameter on the sixteenth day.

(13) *Koh Teck*.—A male with latent tertiary syphilis. He had received very little mercurial treatment. His serum gave a positive Wassermann reaction, deviating ten units of complement.

On the day following the injection of luetin there was, at the site of inoculation, a round papule the size of a split pea without any surrounding inflammation. It increased in size and, on the fourth day, it was red, inflamed itching and rather painful. It measured nearly 1 cm. in diameter. On the sixth day softening was observed in the centre; an abscess formed, covered by purple, congested skin and, for twenty-four hours or so, the patient felt ill and feverish. The contents of the pustule became absorbed, so that on the eleventh day all that remained was a small, raised, dark-coloured patch covered with scaly epidermis. This gradually disappeared leaving a pigmented scar.

(14) *Sia Tiap*.—A male with latent tertiary syphilis. His serum gave a negative Wassermann reaction. He stated that his leg had been amputated for venereal disease. He had numerous syphilitic scars.

On the day after the injection of luetin there was a red papule at the point of inoculation. On the sixth day this had become a red furuncle 2 cm. in diameter. This remained stationary for a week and then began to subside. By the twentieth day all swelling had disappeared, but there was a small scab where the furuncle had been.

(15) *Chang Yeong*.—A male with latent tertiary syphilis. His serum gave a weak, positive Wassermann reaction, deviating five units of complement. He stated that his leg had been amputated for venereal disease and he bore on his body the marks of many syphilitic scars. The luetin reaction was of the pustular type.

#### C.—TORPID FORM.

(16) *Ah Ho*.—A female with latent tertiary syphilis. Some years ago she received several courses of mercurial inunctions. Her serum was not obtained for the Wassermann reaction.

In her case, the inoculation of luetin produced a torpid, papular reaction. A small papule appeared about the tenth day which disappeared in a little more than a fortnight, leaving a small pigmented mark.

(17) *Chin Sang*.—A male with latent tertiary syphilis. His blood gave a weak, positive Wassermann reaction, deviating five units of complement. He had been blind for ten years from the effects of some acute inflammatory affection of the eyes. He stated that he had syphilis twenty years ago.

The small papules produced by the injection of the luetin and control inoculations both disappeared; but on the twenty-first day a papule appeared at the site of the luetin injection which in five days had increased to 1 cm. in diameter and was fluctuating in the centre. Ten days later there was an oblong, fluctuating abscess which measured 3 cm. × 2 cm.

(18) *Foong Wey*.—A male with latent tertiary syphilis. His blood gave a negative Wassermann reaction. He had been blind for several years from the effects of some acute inflammation of the eyes. He had suffered from syphilis.

The minute papule caused by the injection of luetin persisted for some time, but there was no definite positive reaction until the fifteenth day, when the papule became inflamed, increased in size and softened in the centre. Five days later this abscess burst and the inflammation disappeared leaving a small pigmented patch.

(19) *Lee Soon*.—A male with latent tertiary syphilis. He had been blind for five years; the result, apparently, of some form of acute ophthalmia. He was unwilling to have his blood examined. There was a history of syphilis.

After the injection of luetin there was no immediate reaction, but a small papule appeared at the end of the second week. On the twenty-second day this was about 5 mm. in diameter and gave rise to slight irritation. It never softened or became any larger and it gradually disappeared.

(20) *Chong Fat*.—A male suffering from double optic atrophy associated with loss of knee-jerks. His serum gave a positive Wassermann reaction, deviating more than ten units of complement. On the eighth day a small papule appeared which persisted for more than three weeks but never suppurated.

(21) *Phung Nghee*.—A male with latent tertiary syphilis. His serum gave a negative Wassermann reaction. He had been blind for many years from the results of an acute inflammation of the eyes.

The little swelling produced by the inoculation of luetin disappeared on the following day, but, nine days later, a papule appeared which became inflamed and suppurated. It ruptured and discharged the usual brownish contents when slight pressure was made on the twenty-fifth day.

(22) *Chin Ghan*.—A male suffering from double optic atrophy the result of tabes. On his right leg, there were old syphilitic scars. His serum gave a positive Wassermann reaction, deviating more than ten units of complement.

A small papule, not so large as a split-pea, persisted at the site of the luetin inoculation. At the end of a fortnight this papule became a little larger, it remained stationary for several days, then softened in the centre and became inflamed and increased in size, so that on the twenty-fourth day it had become a small fluctuating lump 1.2 cm. in diameter.

#### WATER AND WATER SUPPLIES.

A considerable amount of bacteriological and chemical research has been carried out on existing and proposed water supplies.

As regards existing supplies, the work has been mainly confined to those of Taiping and Kuala Lumpur.

For the enumeration of the organisms present in water, gelatine plates do not yield satisfactory results here. Plates containing +10 nutrient agar have therefore been employed and the estimations made after incubation at 37° C. for forty-eight hours.

By this method the water which is supplied to Kuala Lumpur has been found to yield, in dry weather, an average of forty-five organisms per cubic centimetre. In wet weather the average number was seventy in the same volume of water. The presumptive test for *Bacillus coli* was positive in not less than five cubic centimetres save once. On that occasion the examination was made after heavy rain which had followed on a period of dry weather and a positive result was obtained with one cubic centimetre.

The lactose-fermenters isolated in the dry weather during January and February were *B. cloacæ*, *B. grunthal*, *B. vesiculosus*, *B. lactis aerogenes* and *B. neapolitanus*.

The method employed was that recommended by Major Clemsha who has shown that these organisms belong to the class of coliform organisms which are of a resistant nature and not necessarily indicative of recent pollution.

The results obtained in October and November, after heavy rains, were not so satisfactory. *B. coli communis* (*Escherich*) and *B. coli mutabilis* (*Massini*) were isolated on these occasions from ten cubic centimetres of the water.

On one occasion an unsatisfactory condition of the new water supply was reported and eventually traced to the presence of illicit mining on the catchment area; this was stated to be rigidly reserved and patrolled.

An unsatisfactory condition of the filtered water supplied in Taiping was detected here and, on investigation, proved due to inefficiency of the filters. It is of interest to note that the communication received with the sample of water stated that everything in connection with the water supply was satisfactory.

As regards projected water supplies these have been mainly concerned with a low lying, sparsely populated district in Perak and a low lying district in Selangor. In the former case the water to be employed might fairly be described as dilute sewage; in the latter case it is dilute sewage mixed with a large amount of colloidal clay.

It is proposed in both cases to employ mechanical filters in order to obtain a potable water.

The hills are for all practical purposes free from human habitations. They furnish therefore excellent catchment areas, the distance of which from the point of distribution can in no instance be excessive, it can certainly never approximate to the great distances which are necessary at home for the transport of potable water. The annual rainfall

exceeds one hundred inches. There is therefore no apparent reason why every part of the Peninsula should not be provided with a water supply exceeding in excellence that which can be provided in other and more densely populated tropical countries. It has been contended as regards the sparsely populated area that in no other country would a water supply be provided because the cost would be excessive and the revenue inadequate, but that furnishes no grounds for the provision of a water supply the source of which is known to be unsatisfactory.

On account of the process of elutriation by which tin-ore is produced, the water in the rivers in practically every part of the country contains colloidal clay; the greater the amount of this material present the greater is likely to be the amount of contamination present from human and other undesirable sources. This is well illustrated by the projected source of water supply for a low lying district in Selangor.

It may be that on the grounds of expense and engineering difficulties, water supplies from rivers cannot be brought from these sources at a point above that at which they are systematically subject to contamination, but I can conceive of no circumstances under which it is permissible in this country systematically to arrange for the conversion of dilute sewage into water for human consumption. The fascinating position which filters, mechanical and otherwise, occupy in the minds of many in this country is surprising and it would appear to be considered that the more elaborate and complicated the process by which filtration is accomplished the more excellent must be the results. In densely populated countries and in certain circumstances such methods may be unavoidable, but in this country they are certainly not.

It is true that dilute sewage can be treated in such a way as to render the final product potable. Courageous individuals have on occasion partaken of the filtrate from the contact-beds of a septic-tank system; but a proposal to make that system the regular source of a potable water supply would meet with objections amply justified on grounds other than sentimental. By chemical precipitants and mechanical filters undesirable materials can to a large extent be removed from waters. This is more especially true in the case of hard waters. In those waters the lime contained forms with the added alum a precipitate which is easily got rid of. In this country there are no hard waters. The colloidal clay contained in the waters forms with the alum a jelly-like mass which is difficult to remove and clogs the filters, thus necessitating an amount of care which must imperil their efficiency.

Every process of mechanical filtration requires constant skilled care and attention; this cannot be obtained under the conditions which prevail here.

Even granting that the major portion of the undesirable material has been removed, an undesirable portion remains and there is the ever present danger that through some fault this may be increased.

Recently a case came under our notice which illustrates the danger which may arise from the use of mechanical filters in this country. The water supply of a large town has hitherto been purified by the use of sand-filters. It was considered possible that by means of mechanical filters an equally if not more satisfactory filtrate would be obtained and an economy in cost effected. The raw water contains a sufficient amount of suspended material to render it faintly opalescent but that opalescence is not removed as a precipitate by the use of alum. Consequently the water after passing through the mechanical filter was still opalescent and contained the most of the added alum. It was next attempted to remove the opalescence by the addition of a small quantity of soda-ash, but this substance causes the suspended matter to pass into solution and the water is cleared. The mechanical filter is therefore deprived of what is claimed to be an essential part of the process and it is obvious that for this water its use is not permissible.

Already investigations have been made on water from the hills, this work it is proposed to extend with a view to obtain reliable information and to urge the desirability of obtaining water supplies from the numerous excellent sources which must exist in place of from the undesirable sources to which so much attention is now being devoted.

#### THE PRECIPITIN TEST.

This reaction was only called for on three occasions. In one case of alleged murder a knife stained with mammalian blood was submitted for examination because it was contended by the defence that the stains were caused by pig's blood. At that time no anti-pig serum was available, but we were able to determine that the stains were not caused by human blood. Since then the varieties of precipitating sera have been largely increased and we are now in a position to deal with almost every contingency which may arise.

The other two cases were of no special interest, the blood-stains in both were satisfactorily proved to have been caused by human blood.

#### WIDAL REACTIONS.

The widal test for typhoid fever was applied in 184 cases, of which 53 gave a positive result; for paratyphoid fever in six cases, all of which were negative.

#### CHOLERA, DIPHTHERIA AND OTHER ROUTINE EXAMINATIONS.

Material from twelve cases, suspected to be cholera, were submitted for examination. In only one was the specific organism of Asiatic cholera isolated.

Five specimens were examined for the presence of *B. diphtheriae*, all were negative.

Four specimens were examined for the presence of *Meningococcus* with a negative result in each case.

Blood films from 156 cases were submitted for examination in doubtful cases of malaria, filariasis, blackwater fever, piroplasmosis of animals, etc. In two cases the presence of *Babesia* was noted in recently imported Australian cattle.

Other examinations included sputum for tubercle bacilli, pus smears for gonococci, faeces for ova of helminths, amoebae, identification of helminths, seminal stains in medico-legal cases, etc.

#### RABIES.

The brains of eight dogs, suspected of rabies, were examined for Negri's bodies. The results were positive in four cases; two of which occurred in Raub during April, the third in Kuala Pilah, on the 16th of September, and the fourth in Malacca about a week later.

#### MULTIPLE TERATOMATA IN A GIBBON.

This animal, previously referred to in connexion with leprosy, died on the 21st January, 1913, and an autopsy was performed two hours after death.

At the site of inoculation there was a slight scar and subjacent a small nodule about the size of a millet seed could be felt. On incision the adjacent tissues showed no inflammatory reaction.

Over the costal cartilages of the right third and fourth ribs there was a lobulated tumour the size of a walnut. The skin was freely movable over the tumour. On removing the skin and freeing the tumour, it was found to be adherent to the costal cartilages mentioned above. The tumour felt hard. The thorax was opened. There was no extension of the tumour into the thorax. The thoracic contents were removed. A tumour the size of a bean was seen in the first left intercostal space about midway between the sternum and the spinal column. In the same intercostal space close to the vertebrae there was a tumour the size of a pea. In the first and second right intercostal space close to the vertebrae there were tumours of similar size. In the eleventh right intercostal space, close to the vertebrae there was a tumour the size of a filbert.

The abdominal contents were removed. Over the lumbar vertebrae and towards the right side there was a tumour the size of a walnut. In the left psoas muscle, near its upper fibres of origin, there was a lobulated tumour the size of a coffee bean. Each tumour on incision was found to contain hair mixed with pultaceous material. The larger tumours contained cartilaginous and bony plates.

On microscopic examination the cystic portions, containing hair and pultaceous material, were found to be lined with stratified epithelium, containing hair follicles and sebaceous glands.

Apart from the intestine, the other organs of the body appeared normal. In the ileum the Peyer's patches were congested and raised. In the large intestine there were numerous minute pin-hole ulcers and granulations.

The immediate cause of death was dysentery.

#### TUMOURS.

Of the tumours examined two were of some interest.

##### 1.—A PRIMARY SARCOMA OF THE LIVER.

On 24th September there were received from the Medical Officer, Kuala Kubu, the liver, spleen, stomach, lung, uterus and heart of a Tamil woman, aged 35. All these organs had been preserved in a solution of formalin. The uterus appeared to be normal. The liver was an enormous irregular mass, with irregular bosses on its surface. It weighed 181 ounces. The normal contour of the organ was lost and the limits of its several lobes were no longer definable. The gall-bladder, which was small and shrunken, contained a little bile. The outer parts of the liver were very tough and hard, but the centre had undergone degeneration and was in a pultaceous, encephaloid condition. No traces of liver tissue could be recognized by the naked eye. The organ appeared to consist entirely of new growth, in which there were numerous haemorrhages and areas of necrotic softening. In histological sections it was seen that the liver consisted of interlacing bands and whorls of large spindle-cells. In some areas there was a moderate development of fibrous tissue, in others, there was necrosis. The tissue was nowhere very vascular. In a few places there were strands of necrotic liver cells.

The lungs appeared to be normal except for the presence of a few small nodules on the surface which were about the size of miliary tubercles but less well defined. The examination of microscopical sections showed that the lungs were full of metastatic deposits, similar

in structure to the new growth in the liver. These occurred in the deep layer of the pleura, in the adventitia of the blood vessels and bronchioles and in the septa. These deposits were nearly all of microscopic size; they were not encapsulated, but merged with the surrounding tissues so that their limits were ill-defined. The capillaries of the lung were slightly congested, but the deposits of new growth excited no localized inflammatory reaction, they were surrounded by no small cell infiltration.

On the surface of the spleen there were a few small white nodules less than 1 cm. in diameter. These consisted of new growth similar to that found in the liver; the tissue in the centre of each had undergone degeneration. The nodules were well defined but they were not encapsulated, they appeared to have pushed aside the tissue of the spleen.

On the outer surface of the right auricular appendix there was a small white nodule 2 mm. in diameter. The structure of this was the same as that of the other growths.

Within the stomach, on its posterior wall, there were three flat, umbilicated, white nodules, the largest of which measured 1 cm. in diameter. These tumours were of the same nature as those already described. They were sharply demarcated from the surrounding tissues, which they did not infiltrate, but had thrust aside in their growth. They were imbedded in the mucosa which overlapped their margins but was not continuous over their free surfaces which projected into the cavity of the stomach. They were superficial to the *muscularis* which had atrophied beneath them.

The chief point which arises in connexion with this case is whether the primary growth had its origin in the liver or in the stomach. The new growth in the liver had entirely destroyed the tissues of that organ except a few strands of degenerate liver cells near the surface; the centre of the viscous was necrotic and semifluid. The growths in the stomach were small, they had undergone no degeneration and they were not fibrotic. These are points in favour of the tumour in the liver being the parent growth, yet it is difficult to see how a primary growth in the liver could give rise to metastatic deposits in the mucosa of the stomach, while the reverse occurs frequently. The spindle-cells in some parts of the tumours were very large so that it was a matter of difficulty to decide whether they were fibres of unstriped muscle or only large spindle-cells. It is possible, therefore, that the primary growth may have been a malignant myoma of the stomach. On the other hand, the small size of the gastric tumours, the absence of degeneration or differentiation into fibrous tissue and the absence of ulceration over them are all points in favour of the liver tumour having been the primary growth.

## 2.—TUBERCULAR GLAND AFFECTED WITH SARCOMA.

A Chinese, with profuse haemorrhage from a tumour in the naso-pharynx, was admitted to Batu Gajah Hospital and died a few hours later. A portion of the tumour (a spindle-celled sarcoma) and an enlarged lymphatic gland from the neck were sent to the Institute by Dr. Dowden, the Medical Officer in charge of the hospital. The gland was a pathological curiosity, for while one of two contiguous lymphatic nodules was infected with tubercle and contained giant-cells, the other was composed of sarcomatous spindle-cells.

## CHEMICAL EXAMINATIONS AND INVESTIGATIONS.

The total number of articles examined during the year was 1,067 as compared with 1,236 during the year 1912.

They may be classified as follows:

1. Criminal investigations	...	...	...	...	...	...	50
2. Toxicological analyses	...	...	...	...	...	...	58
3. Opium and chandu	...	...	...	...	...	...	74
4. Chandu dross	...	...	...	...	...	...	11
5. Deleterious drugs (morphine and cocaine)	...	...	...	...	...	...	157
6. Waters	...	...	...	...	...	...	99
7. Milks	...	...	...	...	...	...	225
8. Tinned milks	...	...	...	...	...	...	2
9. Alcoholic liquors	...	...	...	...	...	...	70
10. Counterfeit coins and materials	...	...	...	...	...	...	270
11. Miscellaneous analyses and special investigations.	...	...	...	...	...	...	51

## 1.—CRIMINAL INVESTIGATIONS.

Under this heading are comprised the examination of various articles such as knives, parangs, weapons, articles of clothing, etc., for blood stains.

In two cases, the stains of mammalian blood were identified, by the precipitin test, as those of human blood. The total number giving positive results was thirty-nine. In the majority of these cases evidence as to the results was given in Conrt.

## 2.—TOXICOLOGICAL ANALYSES.

On the 58 analyses 24 gave positive results, being an increase on the number of positive results obtained in the previous year.

The poisons found were :

- Arsenic in ten specimens ;
- Morphine in seven specimens ;
- Strychnine in two specimens :
- Quinine in two specimens ;
- Opium in one specimen ;
- Potassium cyanide in one specimen.

In one case of alcoholic poisoning, a small quantity of alcohol was found.

In the two cases of quinine, death, as far as the evidence has proved, has been due to an overdose of quinine.

## 3.—OPIUM AND CHANDU.

There is a small decrease in the number of these examinations. Forty-eight of these samples were found to consist wholly or in part of Government chandu. Eight were found to contain chandu other than that of Government manufacture. In twelve of these exhibits no opium was found, and in the remaining six opium was found to be present. In some cases the amount of morphine was estimated.

Prosecutions resulted in the majority of these cases.

## 4.—CHANDU DROSS.

Eleven samples were received during the year and the number of samples examined in 1912 was 97. The decrease is mainly due to the fact that it was found impossible to say whether the dross was wholly or only in part derived from Government chandu.

Seven of these samples were derived from chandu of Government manufacture.

## 5.—MORPHINE AND COCAINE.

The number shows a large increase, and the number of exhibits containing morphine hydrochloride was 135. One sample was found to contain morphine sulphate, and two samples cocaine hydrochloride. In most of the cases where morphine hydrochloride was found, sugar was also found as an adulterant; the sugar being as a rule lactose, a tasteless white powder.

Nineteen samples gave negative results.

## 6.—WATERS.

There was a small decrease in the number of waters analysed. The systematic examination of the Taiping supply was continued.

In January the waterworks at Taiping were visited owing to the presence of algae in the supply.

The supply reservoir was found to contain a fair quantity of algae, and instructions were given to clear out the supply reservoir and also the filter wells. From that date the water has maintained a satisfactory degree of purity. Other samples examined were those of Kuala Lumpur, Seremban, Kuantan, Kuala Lipis, Gemas and Kajang.

Many samples from the Railways were also examined, the majority being required for boiler purposes.

## 7.—MILKS.

A great decrease in the number of milks examined compared with the year 1912.

The number found to be adulterated was 32 and the highest percentage of added water was found to be 66 per cent.

Evidence of adulteration was given in Court in most of these cases and the offenders fined.

A systematic investigation of the milk supply of Kuala Lumpur was begun, but owing to Mr. J. R. Hill being on leave, this work had to be discontinued.

The investigation was undertaken with a view to obtaining a standard for milk in Kuala Lumpur.

The milking sheds surrounding Kuala Lumpur were visited and the samples were taken from the actual quantity of milk obtained from the cow, thus obtaining an unadulterated and true sample of the milk.

## 8.—TINNED MILKS.

Two samples of tinned milk were analysed and found to be of good quality.

## 9.—ALCOHOLIC LIQUORS.

Seventy alcoholic liquors were examined during the year compared with 106 in the previous year.

Twenty-two samples were examined completely. Twenty-seven were partially analysed, the majority for spirit strength only.

Twenty-one samples of toddy were examined, and the highest quantity of alcohol found was equivalent to 15 per cent. proof spirit. Two samples of alleged toddy were found to contain no alcohol.

## 10.—COUNTERFEIT COINS AND MATERIALS.

One hundred and seventy-seven coins were examined, five of these were found to contain the correct proportion of silver, none of the remainder contained any silver but consisted of an alloy of antimony and tin. Fourteen moulds were received, the majority contained metal.

Britannia metal spoons were also examined and found to consist of an alloy of antimony and tin.

Solutions of nitric acid and potassium cyanide were also examined.

## 11.—MISCELLANEOUS ANALYSES AND SPECIAL INVESTIGATIONS.

Under miscellaneous samples were included, samples of an accumulator deposit, anti-opium pills, galena, "ganja," dyes, cloves, "rengut," rice, seeds, and an estimation of arsenic and sulphur dioxide in the flue gases of a furnace.

Among the special investigations which were undertaken were the analyses of various samples of unadulterated milk already described under the heading of milks.

Some Malay medicines were examined with a view to discovering if they had any medicinal properties, no alkaloidal or other substance was found to be present, which could be said to have medicinal properties.

## PUBLICATIONS.

In the *Lancet* of the 10th January a communication on "Unpolished Rice and the Prevention of Beri-beri" was published.

A paper entitled "The Bacillus Lepræ: has it been cultivated?" was presented to the Seventeenth International Congress of Medicine and published in the *Lancet* of the 27th September.

A communication entitled "The Anopheles of Malaya, Part I (*Anopheles tessellatus*, Theob.)" was contributed to the *Bulletin of Entomological Research* by Dr. Stanton who also contributed a paper entitled "Anopheles and Malaria in the Oriental Region" to the Third Biennial Congress of the Far Eastern Association of Tropical Medicine. The latter paper will appear in the transactions of the Congress.

## STAFF.

Dr. Stanton returned from leave and resumed the duties of his appointment on the 21st February.

Mr. Hill was appointed to the post of Assistant Chemist in the Department of Agriculture on the 4th June, but he continued to hold the post of Chemist in this Institute until the 3rd October when he proceeded on leave.

Mr. Blair was promoted to the post of Chemist, but a successor to Mr. Blair had not been appointed at the close of the year.

There have been several changes in the subordinate staff caused by retirement and transfer, but the vacancies have been suitably filled.

H. FRASER,  
Director, Institute for Medical Research, F.M.S.

## REPORT OF THE MALARIA ADVISORY BOARD FOR THE YEAR 1913.

1. A report on the work of the Malaria Advisory Board for the year 1912 was included in the Medical Report for that year; a brief description of anti-malarial work carried out in past years, more particularly in Kuala Lumpur, was given and the urgent necessity of a general campaign against malaria which led to the appointment of the Board in November, 1911, was remarked on. Since that time the need for this general campaign on proper lines under centralized control has become even more evident.

Some misapprehension as to the functions of the Board, and a lack of knowledge of the work it has carried out and the programme before it, still prevails, and information on these points is given in what follows.

2. Before the establishment of the Board many attempts were made in various localities to reduce malaria, in some instances with a fair measure of success, but in no case with the exceptions mentioned later was the improvement completely maintained. In most instances the work failed to effect any improvement, and in many where drainage work was attempted the evil actually increased. The reasons for failure where drainage work was attempted were that the work was not done thoroughly nor maintained in a proper way. Where quinine prophylaxis was tried it gave very varying results as no machinery exists which would ensure thoroughness. A further reason for failure lay in the constant changes in the holders of various appointments concerned with anti-malarial work.

3. In order to obviate the difficulties which led to failure it was evident that provision must be made for continuity of policy and extreme thoroughness in carrying out anti-malarial measures. These factors are of course essential to success in any work, but their neglect or partial neglect produces particularly bad results when dealing with malaria prevention. The Board was appointed in order to ensure that these factors would be observed and to obtain and review information with regard to malaria so that a satisfactory and economical policy could be decided upon. The Board has collected much information with a view of obtaining a closer knowledge of the causes, incidence, and effects of malaria.

4. The Travelling Medical Entomologist, Dr. C. Strickland, who began work in May, 1912, has visited a large number of places in the Malay States for the purpose of studying the life history and habits of the anopheline mosquitoes. He has written certain pamphlets dealing with mosquitoes and compiled a most useful "Short Key to the Identification of the Anopheline Mosquitoes of Malaya for the use of Medical Officers and Others" which was printed by the Government Printing Office, Kuala Lumpur, in 1913. This has been distributed to those known to have interest in the subject, and copies may be obtained on application.

At the request of the Board, Government has arranged for a building at Bukit Nanas, Kuala Lumpur, to be used as a Malaria Bureau. The work on this building was nearly completed at the close of 1913 and it should be in use early in 1914. The bureau will serve as head-quarters for the Travelling Medical Entomologist, and laboratory work in connection with his studies will be done there. It is intended that a library and museum of exhibits shall be formed and that the bureau shall be available for instruction in, or study of, the subject by those interested.

The Bacteriologist at the Institute for Medical Research, Dr. A. T. Stanton, has continued his work in connection with the biology of mosquitoes and has published a number of papers relative to this.

The Board hopes that practical advantage will result from the studies of Doctors Stanton and Strickland.

5. The Board considered it of importance that the population generally should be better educated with regard to malaria, and to this end the now well-known pictorial card was issued widely, printed in English, Malay, Chinese and Tamil characters. It is inevitable that such a card should be misunderstood by certain classes, but this attractive production has well served its purpose in calling general attention to the causation, prevention and treatment of malaria. An uncoloured reduced facsimile of the card is appended (plate I). Notes for elementary lectures on the subject which it is intended shall be given in all schools, using the pictorial card as a means of illustration, have been prepared, and arrangements have been made for lessons to be given. There is very great difficulty in translating the simplest scientific ideas into the language of people who have no general elementary knowledge of science in such a way that the ideas shall be easily understood, and differences of opinion amongst authorities on the various vernaculars has occasioned some delay.

6. The Board aims at the extermination of anopheline mosquitoes in all thickly populated centres and, wherever economically possible, in rural areas, and wishes to effect a reduction of mosquitoes generally. The means it has decided shall be adopted for these purposes in the light of present knowledge are:

- (a) Land drainage and clearing of drained areas;
- (b) Reduction of breeding in lakes, rivers and other large bodies of water, by removal of weeds and algae from shallow places;

- (c) Removal of bottles, tins, boxes, shells or any other waste articles likely to hold water, and the screening of all tanks, wells, or water-containing vessels;
- (d) Periodical use of oil or larvacides on breeding places not otherwise dealt with; and, as a matter of the utmost importance,
- (e) Efficient upkeep of all anti-malarial works.

At present the only permanent and really satisfactory measure is that under (a) above, supplemented by (b), (c) and (e). It is also, in the majority of places to be dealt with, the most economical. Close study of the subject will it is hoped lead to a cheaper and easier means being disclosed, but the scientific work available to the Board at present offers no better solution. The drainage work carried out by the Executive Engineer to the Board and its effect will be referred to in detail later.

7. The Board took steps to further the distribution of quinine wherever malaria is prevalent and particularly in places far from hospitals or dispensaries. It was considered that tabloid quinine bihydrochloride was the best form for general distribution, and a large supply was obtained in tubes each containing twenty 4-grain tabloids, with a printed wrapper giving directions for its use in English, Malay and Tamil characters; and a quantity of these have been sent out to various local authorities for distribution free of charge by penghulus, police and others at the discretion of the local authorities. Very favourable reports have been received of its use and it seems to be in great demand.

8. The Board has been reluctant to advocate the use of plenary powers in connection with anti-malarial schemes until the public generally was better educated in the subject, as much depends on individual effort, and it would not be possible without restrictive laws of an oppressive nature and a very large staff of inspectors to see that they were obeyed, to obtain much result from the use of such powers. It has now become obvious however that an Enactment to allow of anti-malarial works being carried out on alienated land is necessary. An illustration of this necessity is the case where a small estate, the owners of which are desirous of carrying out anti-malarial work, is surrounded by other estates whose owners object to such work, where work on the small estate would possibly not be of use unless it were extended into the remainder. A Bill to provide for this and to define more clearly the powers of the authorities in connection with remedial measures against malaria has been under consideration for some time, and it is hoped will be put forward shortly.

9. To provide for the effective initiation, control and maintenance of anti-malarial work the Board in 1911 recommended that local Anti-Malaria Committees should be appointed for districts by the Residents in each State. These have been appointed in a few cases only, and the Board acknowledges the active interest displayed by some of the Committees. It is hoped that local Committees will be appointed in all districts and that they will take full advantage of the large opening for extensive and thorough measures made available by Government and of the services of an increased executive staff attached to the Board.

10. The anti-malarial drainage work carried out by the Executive Engineer to the Board at Kuala Lumpur will now be referred to in detail. The history of the work in Kuala Lumpur and the reasons which led the Board to decide on thoroughly dealing with a particular area were reviewed at length in the Medical Report of 1912. It may with advantage be re-stated however that certain anopheline mosquitoes breed only in certain types of country, and in a general way it has been found that while in flat land open drainage and clearing of jungle may get rid of the pathogenic types of anophelines usually found there, only subsoil drainage is, as a general rule, successful in hill country.

The reasons for this do not lie in any particular virtues possessed by earthenware pipes but in the fact that an open drain or stream in hill land is a suitable breeding place for certain mosquitoes owing to the pools of water and wet patches of ground which form in their channel and along their sides although there may be considerable current of water in these pools. Anopheline mosquitoes have not the characteristics of trout nor are they able to breed in water moving with a high velocity in a channel with edges as smooth as an earthenware pipe because their larvae cannot obtain food in such water unless it is held up by obstructions. The problem of anti-malarial drainage was not to cause water to flow out of sight but to cause it to move in such a way that it did no damage to its channels, and to drain land so that no pools nor wet ground were left.

Flat land and swamp drainage presented no technical difficulties, and it is flat land estates near the Coast which form the exceptions to the general failures mentioned in paragraph (2) above, where draining and clearing over a sufficient area have proved to be entirely effective. Fortunately in these places good drainage is essential from a purely agricultural point of view and this happens to entirely coincide with the measure best calculated to abolish malaria.

The subsoil drainage of ravines in hill land economically was an unsolved problem, and a most important one, as upon its successful solution depended the application of drainage as a radical anti-malarial measure to hill land. As stated in the 1912 report, this problem was solved and the experience gained made it possible to carry out such

work with a certainty of success. Work has since been done in precipitous country which presented extraordinary difficulty at a cost remarkably low, and the Board can now unhesitatingly state that thorough drainage can be applied to any type of land economically with a certainty of success if it is done by those having the necessary experience.

A map is attached (plate II) showing Kuala Lumpur town and environs, on which is indicated the area drained by the end of the year under review. The cost of the work in Kuala Lumpur from 1911 when the Executive Engineer to the Board first took charge of the work to the close of 1913, but including work done previous to 1911 still in use, is as follows :

Year.		Construction.	Maintenance.
1908-1911	...	\$ 47,705.00	... \$ 6,985.85
1912	...	37,526.69	... 5,589.51
1913	...	68,459.36	... 11,118.07
		<hr/> \$153,691.05	<hr/> \$23,693.43

The following quantities of drains were made :

Year.	Masonry drains.	Subsoil pipe drains.	Earth channels for larger streams.
1908-1911	17,415	50,439	—
1912	2,549	97,906	—
1913	8,966	109,186	25,288
Lineal feet ...	28,930	257,531	25,288
		<hr/> 311,749 lineal feet.	

In addition to the expenditure detailed above, the following sums have been expended under the direction of the Health Officer, Kuala Lumpur, by a mosquito brigade, principally in reducing domestic mosquitoes and in clearing edges of streams :

1912.	1913.
\$2,600.12	... \$5,015.33

The work done affects about 3,100 acres, roughly three-quarters of the more densely occupied town area including practically the whole of the hill area, and some work has also been done on the remaining north-east quarter, which consists of flat land with much swamp. The capital cost per acre of town area protected is about \$50, and while an exact figure for this will not be available until the whole town area has been dealt with, the final cost per acre will not exceed this sum. Had no work previous to 1911 been done it could have been carried out for considerably less. The stability of the work continues to give the utmost satisfaction and maintenance costs per acre will become even less in the future, as special efforts can be made to keep down expenditure in this direction with an increased staff.

The results obtained are most satisfactory and demonstrate in a striking manner the advantage of anti-malarial drainage well carried out. Unfortunately the results are still affected by the continued existence of four large swamps, known to breed anopheline mosquitoes, where filling work is in progress under the Public Works Department and which were all in a very bad condition from a malarial point of view at the close of the year. The malarial sickness remaining in the town may fairly be attributed to these swamps as it is in their neighbourhood that cases now occur. A chart is attached (plate III) which shows the true total death-rate, the true malarial death-rate, and the rainfall monthly for the years 1907 to 1913, inclusive. The table below gives the true total death-rate and the malarial death-rate for each year :

Year	1907	1908	1909	1910	1911	1912	1913
True death-rate per 1,000	37.9	43.7	32.3	30.3	39.4	36.7	35.5
Malarial death-rate per 1,000	9.7	10.7	7.7	9.8	9.9	5.8	4.2

It was at the end of 1911 that the work done was first completed thoroughly enough to affect the health of the area drained, and all work done since has been equally thorough. The results are evident from inspection of the chart, the malarial death-rate falling, notwithstanding an increase in death from other causes, from an average of 9.56 per 1,000 for the five years 1907 to 1911, inclusive, to 5.8 in 1912, and 4.2 in 1913. On the assumed population of 56,450 for 1913 (last census 1911) this means a saving of 302 lives in 1913. Malaria, as a rule, does not prove fatal except after many attacks, and this saving in lives therefore represents an enormous reduction in sickness.

While malaria can and will be practically eradicated from Kuala Lumpur, the death-rate from malaria will probably always be significant. All persons who have been in the town for a period of one month are included in the total used for obtaining the true death-rate, and sick persons living outside usually come into town if sickness continues for long; this custom will always make its mark on the malarial death-rate.

11. Further interesting figures are available in the health returns of the Police Dépôt, Kuala Lumpur, for the years 1910 to 1913, inclusive, and a chart is appended (plate IV) showing the percentage of Indian recruits at the dépôt who were treated in hospital or given sick leave for malaria, monthly. The protective works were practically completed during 1912 except for the continued existence of the Batu Road swamp, one of the four swamps mentioned above as being filled under the direction of the Public Works Department, which still affects the health of the dépôt and the town in the neighbourhood most unfavourably.

The average monthly percentages of cases of malaria treated in hospital or given sick leave were 35.75 per cent. in 1910, 57.01 per cent. in 1911, 27.33 per cent. in 1912, and 11.3 per cent. in 1913. Further great improvement will take place when anopheline mosquitoes are no longer able to breed in the Batu Road swamp. These figures mean that in 1911, to take the worst case, every Indian at the dépôt was in hospital or given sick leave for malaria on an average seven times in the year. Very few places can show a sickness rate to compare with this, and when it is remembered that the men are picked healthy Sikhs and Pathans of a high physical standard, it will be realized what the condition of a labour force having a poor physical standard would have been under the circumstances. It may be mentioned that the improvement was obtained notwithstanding the large increase in density of the population at the dépôt subsequent to 1911 when in consequence a large number of the men were without the protection of a mosquito net at night. Quinine has only been given to the men under hospital treatment or to those who come to ask for it.

12. Amongst the Government officers and their servants who live in the drained area to the west of the railway practically no cases of malaria have occurred. This is very satisfactory as the officers and their servants living in this area were repeatedly attacked previous to 1912, when some of the bungalows lay empty at times because officers preferred not to live in them, despite a shortage of bungalow accommodation.

13. That the improvement has been due to the works undertaken is proved by the fact that malaria still persists in the neighbourhood of the swamps within the town area now being filled, and on the limits of the area drained two striking examples are :

(a) In the new bungalows at the Experimental Plantation which came into occupation at the beginning of 1913 nearly all the occupants were attacked, but since the middle of the year, when the work in this neighbourhood afforded definite protection, no new cases have occurred ;

(b) Two hundred Tamil coolies who had not suffered from malaria during 1912 were put in temporary lines just within the western limit of the drained area early in 1913. They were attacked so severely that all had to be removed elsewhere, and Chinese coolies were sent to the lines. These also were severely attacked and the lines have had to be abandoned. Estate coolies living in lines immediately to the south of the drained area were severely affected by malaria during the year, and the estate authorities are now carrying out a drainage scheme to protect these lines.

14. In the light of the large reduction in malarial sickness following the measures undertaken as shown in the foregoing remarks, and the rational nature of the procedure which has been adopted, it may be considered that the case for the benefit to be obtained from anti-malarial drainage well carried out has been completely proved, and the Board has every reason to be satisfied that its policy is entirely justified in this respect.

15. The work in Kuala Lumpur was visited by a few officers and a large number of others interested in anti-malarial work, and many of these have already made excellent use of the knowledge so gained

16. Reports have been received on anti-malarial work carried out in each State by the local Committees independently of the Board.

Funds were provided for anti-malarial drainage at Batu Gajah and Gopeng, but these were not spent as the Board were unable to detail an Assistant Engineer for the work. Extensive anti-malarial work is required urgently in Taiping, Kuala Kangsar, Salak North, Sungai Siput, Ipoh, Batu Gajah, Gopeng and Tapah, as well as smaller schemes elsewhere.

17. Having in mind the great advantage to the community of a demonstration on a malarious estate of the possibilities of anti-malarial drainage, the Board has had under consideration for some time the possibility of effecting this. Early in 1913 a Committee was appointed to report on the question with particular reference to the estates between Seremban and Tampin. The Committee visited the district and found that only the Anglo-Malay Rubber Company, the owners of Terentang and Ayer Angat estates, were completely prepared to allow the demonstration to be carried out. Both of these estates are intensely malarious and the Company had for some time gone to considerable expense endeavouring to improve the health of their labour force.

Terentang Estate was eventually selected as having the most suitable features for the demonstration, and after approval by the Board and Government a scheme for thoroughly draining an area on the estate within a distance of half a mile of a central

line site was prepared by the Executive Engineer. At the time of writing this has been approved by both Government and the Company and work will shortly commence and should be completed well before the close of 1914. Owing to the special features of the case and the presence of a river too large to pipe economically running through the area and the Company being required to comply with certain conditions, the work will be paid for partly by the Company and partly by Government. The results of the demonstration will be made public periodically and should prove of great utility to the community in general.

18. The Executive Engineer has been called in to advise in connection with the engineering features of drainage schemes on a large number of estates and reports that in most cases the work since done has been satisfactory. It is to be expected that when the advantages and economy of anti-malarial measures are more widely realized, greater demands will be made for the services of the executive staff in this direction.

19. The Board is satisfied with the results obtained by the work with which it has been intimately associated, but will only be able to look forward to the feature with confidence if adequate steps are taken to ensure that its policy is closely followed and sufficient staff is provided to deal with the places needing urgent attention.

This country is in an exceptional position amongst British Colonies and Protectorates with regard to the measures taken to combat malaria and the Board are naturally anxious that this leading position shall not be lost.

Improvement following subsoil drainage done by Government in the Malay States has resulted so far in one place only—Kuala Lumpur—and this work should be followed up by extensive work in various towns and districts in these States, to convince other countries of the benefits to be derived from, and the confidence of Government in the work. Malaria is the greatest difficulty of existence in the tropics, and its successful eradication, even in restricted localities, is a matter of great moment.

20. The personnel of the Board at the close of the year was :

Sir Edward L. Brockman, K.C.M.G., *Chief Secretary, President*

Dr. C. L. Sansom, *Principal Medical Officer, Vice-President.*

Mr. F. D. Evans, *Public Works Department, Executive Engineer.*

Dr. A. T. Stanton, *Bacteriologist, I.M.R.*

The Hon. Mr. W. F. Nutt, *Member of Federal Council.*

Dr. Malcolm Watson.

Mr. H. R. Quartly.

